

# THE MEDICAL CLINICS OF NORTH AMERICA

VOLUME 3

NUMBER 4

CLINIC OF DR. HENRY A. CHRISTIAN

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## DEFECTS IN MEMBRANOUS BONES, EXOPHTHALMOS AND DIABETES INSIPIDUS; AN UNUSUAL SYNDROME OF DYSPITUITARISM

THE case that I am going to show appears to be almost unique, and is reported primarily for the rarity of occurrence of the extraordinary defects in the skull bones, which, with the associated exophthalmos and diabetes insipidus, makes a truly remarkable clinical picture. The diabetes insipidus and its reaction to pituitary substance make certain a causal relation between a functional derangement of the pituitary gland and the increased urinary output. The fact that the only 2 additional cases with similar skull defects which I have been able to find reported in the literature had evidence of disturbed pituitary function makes it probable that the bone changes, too, owe their origin to dyspituitarism. Hence in discussing this case we are calling attention to an effect of pituitary change not generally recognized. Finally, this case has given the opportunity to make observations on the effects of pituitary substance given in various ways.

The patient, A. S., Med. No. 7945, a little girl aged five years, was admitted to the Peter Bent Brigham Hospital on January 24, 1918, referred by Dr. Thomas E. Lilly, of Shirley, Mass. She remained under observation in the hospital for six months. Her history is as follows:

**Family History.**—Father, mother, and one brother are living and well. The brother, who is three and a half years old, is

normal in every way according to the father's statement. The mother has had no miscarriages. The father has had some rheumatism for about a year. The father and mother are both troubled with pain in their backs. There is no family history of cancer, diabetes, gout, tuberculosis, hemophilia, arthritis, or diseases of the circulatory, respiratory, digestive, renal, nervous, or muscular systems.

*Habits.*—Two to three cups of coffee daily. No tea, alcohol, tobacco, or drugs.

*Past History.*—The patient was born in Shirley, Massachusetts, of Austrian parents, and has lived in Massachusetts all her life. She is the first child, and was born at full term after forceps delivery. Her birth weight is not known, but she was of medium size and was breast fed for one year. During this time she grew normally, getting her teeth at the normal time, and had no symptoms of rickets. She had mumps three to four months ago. There have been no other acute illnesses.

*Injuries.*—None.

*Operations.*—None.

*Head.*—For two years she has had pain in her head (see *Present Illness*). No trauma to head. *Eyes:* No failing vision or glasses. Her eyes occasionally become reddened and pain her much of the time. *Ears:* For two years her hearing has been getting poorer. No pain in ears, discharge, or tinnitus. *Nose:* Not subject to head colds. No discharge or epistaxis. She breathes through her mouth all the time. *Teeth:* Her first teeth came in all right, but when she was three years old they began to decay. Several of her second set are now through (see *Present Illness*). *Throat:* No tonsillitis, sore throat, or hoarseness. Her mouth, especially around the teeth, has been sore much of the time for two years (see *Present Illness*).

*Cardiorespiratory.*—No pain in the chest, no palpitation, dyspnea, cough, sputum, hemoptysis, night-sweats, chills, fever, or edema.

*Gastro-intestinal.*—Her appetite is rather poor, but she eats something three times a day. For two years she has had an enormous thirst. Her bowels have been somewhat irregular,

for which Castoria has been used. A movement was obtained almost every day. No nausea, gas, vomiting, hematemesis, distress, colic, icterus, diarrhea, bloody, tarry, or clay-colored stools.

*Genito-urinary.*—For almost two years she has been passing her urine about every hour—from 1 to 2 glassfuls at a time. Her intake is about 9 quarts in twenty-four hours. Three months ago she had a little pain on urination for a short time. No hematuria, pyuria, smoky urine, retention, or incontinence. No history or symptoms of syphilis or gonorrhea.

*Neuromuscular.*—The patient sleeps well. She is of a quiet disposition, not nervous. No vertigo, fainting, twitching, spasms, anesthesia, paresthesia, ataxia, girdle, or shooting pains in the muscles or joints. Her memory is good and her disposition agreeable. Her father says she learns things quickly, talks well, and walks normally. She plays with other children some, but less than a child normally does.

*Weight.*—For the past year she has weighed about 43 pounds, which is the most she has every weighed.

**Present Illness.**—According to the father's statement, the patient was well and normal in every way until she was three years old. At that time her teeth began to decay and become loose and her gums became swollen and tender. No other symptoms were noted. Her mouth continued to be sore, and at the age of three and a half years the right eye became prominent, and she began to drink more water and pass her urine more frequently. These symptoms gradually increased in intensity until both eyes were markedly protruding, and she was drinking 9 quarts of water a day and urinating every hour. She has complained of more or less constant pain in her head for two years. Her hearing has gradually become poorer. Her father thinks she has had no disturbance of vision and she has had no vomiting. For four or five months she complained of a little pain in her back and three months ago she had a little dysuria for a short time. At times her feet and hands become hot and sweaty. (History obtained through father who speaks little English.)

**Physical Examination.**—The patient is poorly developed and nourished, lying quietly in bed and apparently fully conscious. *Skull:* Symmetric. Over the whole skull, but most marked over the posterior portion, are numerous small, smooth irregularities. Both fontanels are closed. In the right frontoparietal region and in the left parieto-temporal region are two irregular areas, each measuring 8 cm. in its greatest extent, which feel soft as compared



Fig. 178.—Front view of head showing the exophthalmos causing a wide aperture between the eyelids.

with the surrounding portions of the skull. Two similar smaller areas are also present in the left frontal region and on the forehead just above the nose. Both pulsate with each heart-beat and bulge when the patient cries; otherwise there is no bulging. The circumference of the head in its greatest diameter is 50 cm. No areas of tenderness. *Scalp:* Clean and free from scars. The veins over the frontal portion are prominent. *Hair:* Brown, fairly abundant, and of fine texture. The *face* gives no evidence

of suffering. It is somewhat triangular in shape with a prominent forehead. The bridge of the nose and the area directly above it are full, rounded, and shiny. The veins of the forehead are prominent and the skin around the inner canthi is cyanotic. The skin is rather pale, of fine texture, normal temperature, and without eruptions or pigment. It is under normal tension and neither dry nor moist. *Eyes:* The pupils are equal, regular, and react to light and accommodation. The sclerae are blue. There



Fig. 179.—Lateral view of head showing prominence of eyeball.

is a slight lacrimation. No photophobia, diplopia, nystagmus, or palsies. There is a very marked degree of exophthalmos (Figs. 178, 179) and lidlag (Von Graefe's sign). The eyes can be held in convergence (no Möbius' sign). The conjunctivæ are rather pale. The eyes are definitely tender. No gross disturbance of vision. No glasses worn. No edema of the lids. Both lids are somewhat reddened, are thin, and the vessels stand out prominently. This condition is slightly more marked on the right. *Ophthalmoscopic examination* is not satisfactory. The

inner margins of the disks are blurred, the outer margins distinct and raised. The veins are tortuous and prominent. *Ears*: The patient hears if one talks in a loud tone. A watch held against either ear is apparently not heard. (The child is very diffident, so this test of hearing is probably not accurate, and later on there was no evidence of deafness. H. A. C.) No stigmata, tophi, or discharge. Mastoid processes not enlarged; no mastoid tenderness. *Nose*: Both inferior turbinates are thickened and the patient breathes through her mouth all the time. No discharge. *Mouth*: The breath is slightly foul. No ulcerations, exudate, or pigment. *Lips*: Of good color and without herpes, ulcerations, or fissures. *Teeth*: The second set of central incisors are through. Several of the other teeth are loose and some are missing. There are a few cavities. All are ill kept. *Gums*: Retracted around part of the teeth and ulcerated, as though about to bleed. Pus can be expressed from along several of them, and the gums in places are coated with a thick, dirty brown exudate. No leadline. *Tongue*: Heavily coated with a light brown coat. The papillæ show up prominently. The tongue is protruded in the median line without tremor. No mucous patches or scars. *Tonsils*: Not seen. *Pharynx*: Covered with the same dirty brown exudate as that on the tongue and gums. Palate and reflexes normal. *Larynx*: The voice is of good quality. *Neck*: No enlargement of thyroid. No palpable lymph-glands. Small pulsations are visible in the cervical vessels. The patient holds her head slightly bent forward and objects to having it lifted or turned sideways. No tracheal tug.

*Thorax*.—Symmetric and expands equally on both sides. It is of normal size and shape. Respiration regular, of moderate depth, and 28 per minute. Pulsations are visible over most of the precordium.

*Heart*.—Apex impulse felt in the fourth space in nipple line. It is regular, forceful, and felt over a large area. The right border is 2 cm. and the left 6 cm. from the midsternal line. A systolic thrill is felt over the whole precordium. The first sound is loud and ringing in character. No murmurs.  $P^2$  is greater than  $A^2$ . No thrills or murmurs over the aortic arch.

*Vessels.*—Radial pulses regular, equal, synchronous, 116 per minute. The vessel walls are not felt.

*Blood-pressure.*—Systolic 90, diastolic 50.

*Lung.*—Tactile fremitus is normally transmitted. No areas of dulness. No changes in voice or breath sounds. No râles. Lower borders of lungs at ninth thoracic spine.

*Abdomen.*—Full, symmetric, tympanic. Fecal material can be felt in the descending colon. No pulsations, tenderness, or spasm. Respiratory movements are plainly visible. No herniae or fluid. Reflexes present.

*Liver.*—Dulness extends from the fifth rib to 1 cm. below the costal margin. The edge is felt and is sharp and not tender.

*Gall-bladder, spleen, and kidneys* not felt. No costovertebral tenderness.

*Genitalia.*—Normal.

*Rectal examination* not made.

*Lymphatic glands* of pea size are palpated in both groins. None felt in the neck, axillæ, or epitrochlear regions.

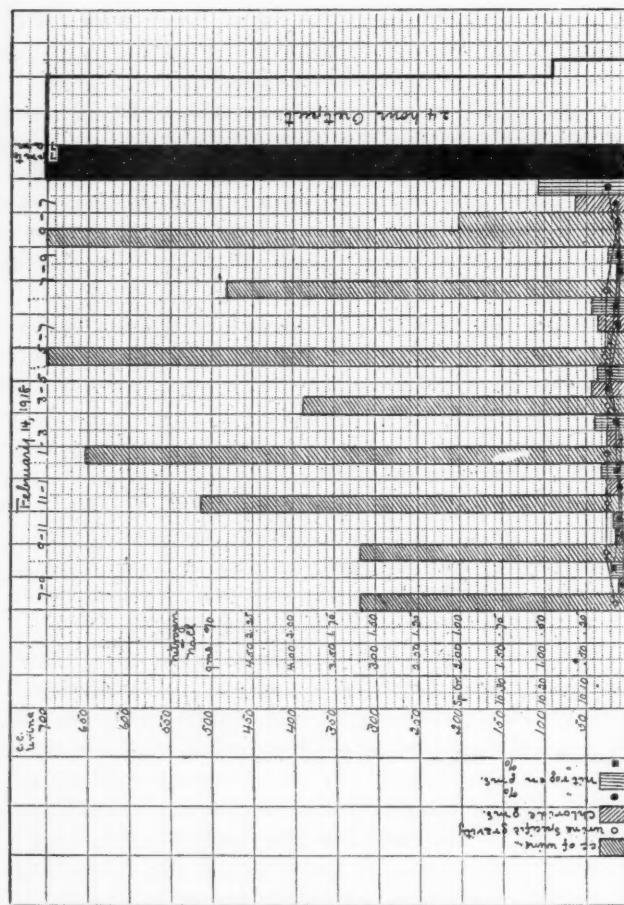
*Bones.*—The spine shows no scoliosis, lordosis, rigidity, or tenderness. No other bones than the skull, as already noted, show any exostoses, irregularities, or tenderness.

*Extremities.*—*Arms* show no involuntary, athetoid, or choreiform movements. The muscles are poorly developed. No tremor or clubbing of the fingers. The nails are not remarkable. The biceps and radioperiosteal reflexes are obtained, but not the triceps.

*Legs.*—No varicosities, scars, or ulcers. Knee-jerks and Achilles' reflexes and plantar reflexes obtained. No Babinski, Oppenheim, ankle-clonus, or Kernig's sign. Romberg and gait not tested. (Subsequently the gait seen to be normal.) No edema. The knees are large.

*Skin.*—No areas of anesthesia, paresthesia, or hyperesthesia.

The Wassermann test on the blood-serum was negative. Study of the stools was negative. Blood examination showed a red blood-cell count of 5,200,000 and a white cell count that ranged between 6600 and 12,600, with an occasional rise to 14,100; 15,600, and 20,100. The differential count on admission



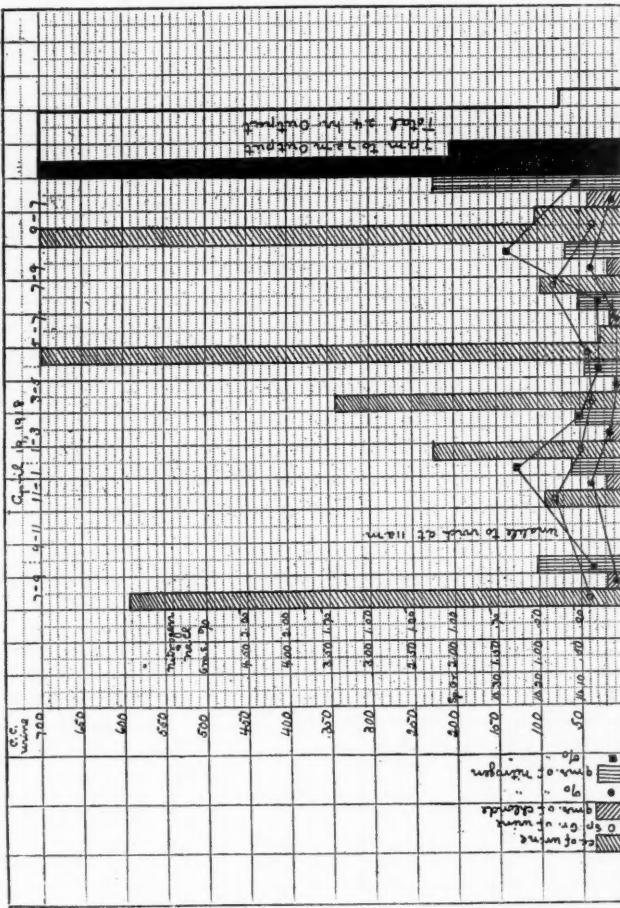


Fig. 181.—Two-hour renal test showing absence of fixation of specific gravity and percentage concentration of sodium chlorid and nitrogen during a period of normal urinary output while the patient was under influence of pituitary substance given subcutaneously. For explanation of the chart see legend under Fig. 180.

showed polymorphonuclear cells 30 per cent., lymphocytes 45 per cent., large mononuclears 23 per cent., and eosinophils 2 per

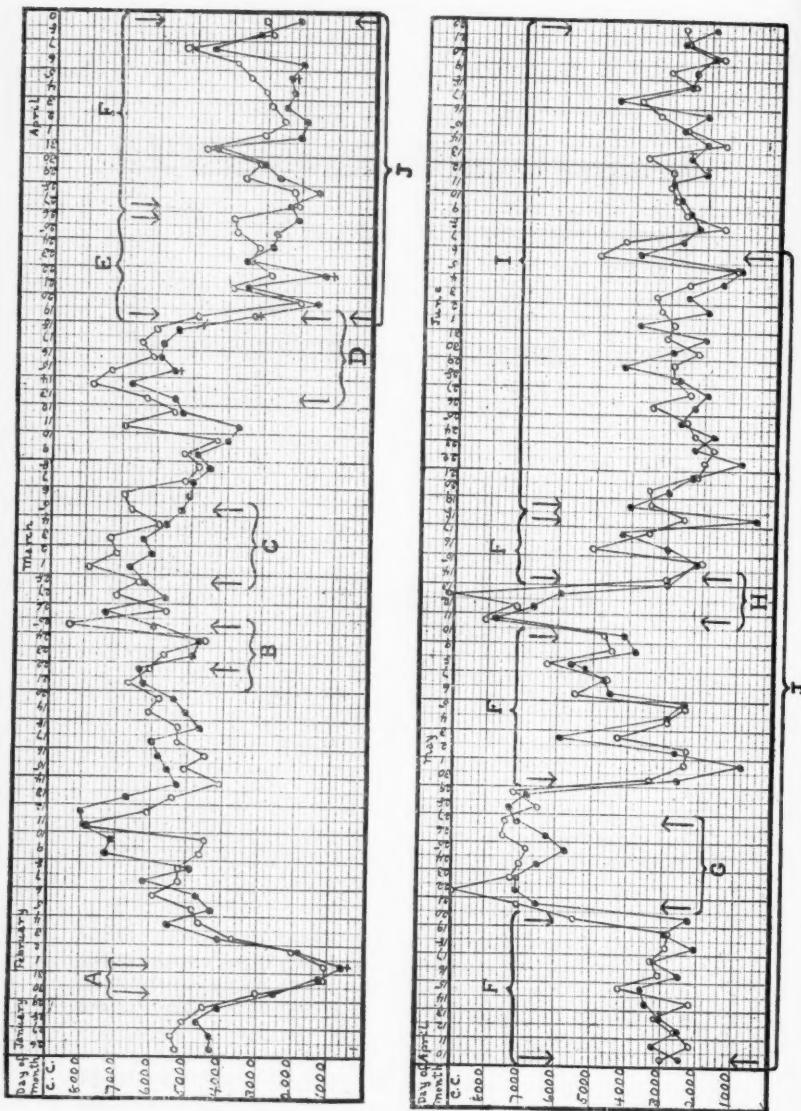


Fig. 182.

cent. The urine was normal except for the low specific gravity during the periods when there was a polyuria. The specific gravity then ranged from 1001 to 1004. Under the influence of pituitary substance, when the amount decreased, the specific gravity of the twenty-four-hour specimen rose to 1008 or 1010. On February 14th, during a period of polyuria with an output of 5250 c.c., a two-hour renal test was made as shown by the accompanying chart (Fig. 180). On April 19th, with a decreased output under the influence of pituitary substance, the output of urine amounting to 2900 c.c., a two-hour test (Fig. 181), in contrast to the first one, shows a very considerable ability to concentrate, as represented by a specific gravity varying from 1007 to 1016, a percentage concentration of sodium chlorid varying between 0.02 and 0.19 per cent., and a percentage concentration of nitrogen varying between 0.13 and 0.69 per cent., as shown in the chart; in other words, a normal picture. In the table

Fig. 182.—Showing fluid intake and urinary output for each twenty-four hours. Letters and arrows refer to pituitary substance given in various ways as indicated below:

- A. Pituitrin, 4 drops subcutaneously three times a day. Begun at 3 P. M. on 1/30 and stopped at 6 P. M. on 2/1.
- B. Dried pituitary gland, 0.1 gram three times a day in gumdrops dissolved in the mouth. Begun at 8 A. M. on 2/22 and stopped at 8 A. M. on 2/25.
- C. Dried pituitary gland, 0.1 gram three times a day in gumdrops dissolved in the mouth. Begun at 8 A. M. on 2/28 and stopped at 4 P. M. on 3/5.
- D. Powdered pituitary gland, 0.1 gram in suppositories four times a day. Begun at 12 noon on 3/13 and stopped at 4 P. M. on 3/19.
- E. Pituitrin, 0.25 c.c. subcutaneously three times a day. Begun at 8.45 P. M. on 3/19 and stopped at 8 P. M. on 3/26.
- F. Pituitrin, 0.5 c.c. subcutaneously twice a day. Begun at 10 A. M. on 3/27 and stopped at 6 P. M. on 4/20. Begun again at 12.35 on 4/30 and stopped at 10 A. M. on 5/10. Begun again at 6 P. M. on 5/14 and stopped at 10 A. M. on 5/18.
- G. Pituitrin suppositories containing 1 c.c. of pituitrin four times a day. Begun at 9.20 A. M. on 4/21 and stopped at 8 P. M. on 4/27.
- H. 2 c.c. pituitrin in 200 c.c. of salt solution per rectum twice a day. Begun at 6 P. M. on 5/10 and stopped at 10 A. M. on 5/14.
- I. Pituitrin, 0.75 c.c. subcutaneously twice a day. Begun at 6 P. M. on 5/18 and stopped on discharge on 6/22.
- J. Powdered pituitary extract by mouth, 0.1 gram four times a day. Begun at 8.45 P. M. on 3/19 and stopped at 12 noon on 6/6.

on page 871 appears the excretion of sodium chlorid and nitrogen from day to day.

The excretion of urine in relation to dosage with pituitary substance was of much interest. Figure 182 shows this graphically. The solid dot represents the urine output for each twenty-four hours; the circle, the fluid intake. The arrows show the time of beginning and ending dosage with pituitary substance. The letters in reference to the key show the form of pituitary substance, dosage, and mode of giving. It is evident in the chart that at *A*, *E*, *F*, and *I* there is a definite decrease in urine output and fluid intake. At those periods the patient received pituitrin (Parke Davis & Co.), a liquid extract of pituitary gland, given subcutaneously in varying dosage. In contrast, gland substance taken by mouth and swallowed, *J*; gland substance mixed in gumdrops and allowed to dissolve slowly in the mouth for local absorption, *B* and *C*; and gland extract (pituitrin, Parke Davis & Co.) in salt solution introduced per rectum, *H*, or in the form of suppositories, *D* and *G*, all failed to have any appreciable effect on the excretion of urine. At no time during the patient's stay was her fluid intake limited; she had free access to water and the fluid intake was such as her sense of thirst dictated. These tests show that pituitary gland substance, in liquid form, introduced subcutaneously, had a striking effect on urine excretion, decreasing it to normal if sufficient gland substance was used, whereas other ways of giving gland substance had a negligible effect. The action of gland substance absorbed from the subcutaneous tissue was temporary, and better effects were obtained by more frequent dosage than by larger doses given at longer intervals. As we shall see later, the quite long-continued use of pituitary substance in this case had no demonstrable effect on the bone defects.

Two determinations of basal metabolism were made on this patient for us by Miss E. H. Tompkins in the Hospital Respiration Laboratory. Her results were as follows: March 11, 1918: Height, 101.3 cm.; weight, 12.5 kg.; buccal temperature, 99.0° F.; blood-pressure—systolic 80, diastolic 50.

	Period I.	Period II.	Average.
Pulse.....	131	130	131
Respiratory quotient.....	0.78	0.78	0.78
Calories per square meter per hour...	57.9	55.4	56.7

*March 29, 1918:* Height, 101.6 cm.; weight, 12.7 kg.; buccal temperature, 99.8° F.; Blood-pressure—systolic 85, diastolic 50.

	Period I.	Period II.	Average.
Pulse.....	119	127	123
Respiratory quotient.....	0.81	0.82	0.82
Calories per square meter per hour...	53.2	56.0	54.6

Miss Tompkins' interpretation of the results appear in the following notes:

*March 11, 1918:* "As yet I can find no standard metabolism for children below eight years of age. At that age it is 54 calories per square meter per hour. From eight to fifteen years the standard metabolism of females changed 3.5 calories per square meter per hour for each year. Assuming the same rate from five to eight years (a very uncertain assumption) the standard for five years of age would be 61 calories per square meter per hour. In this case the child's metabolism would be: Period I = -5 per cent.; Period II = -9 per cent.; Average = -7 per cent. It is worthy of note that the child's pulse was much higher during the determination than it runs on the ward."

*March 29, 1918:* "Metabolism percentage from normal, with the same uncertainty in the standard used, as is noted upon the determination of March 11th: Period I = -13 per cent.; Period II = -8 per cent.; Average = -11 per cent. Here also the pulse runs higher than upon the wards."

It would seem from these reports that no great departure of basal metabolism from the average normal was present. Apparently there is a moderate decrease in activity of metabolism. This would be in complete accord with our usual findings in adults with disturbances of pituitary function, but owing to the uncertainty as to a normal value for such a child it can be regarded quite as much as an essentially normal value of no diagnostic significance.

The most remarkable feature in this case is the truly ex-

traordinary picture revealed by *x*-rays. A number of plates were made during the six months' observation; several times stereoscopic plates were taken. Rather than giving a description of these individual plates a composite description of the group will be attempted. Fortunately, a year before admission (February 22, 1917) she came to the hospital and skull plates were made. These showed at that time a similar, though slightly less extensive process.

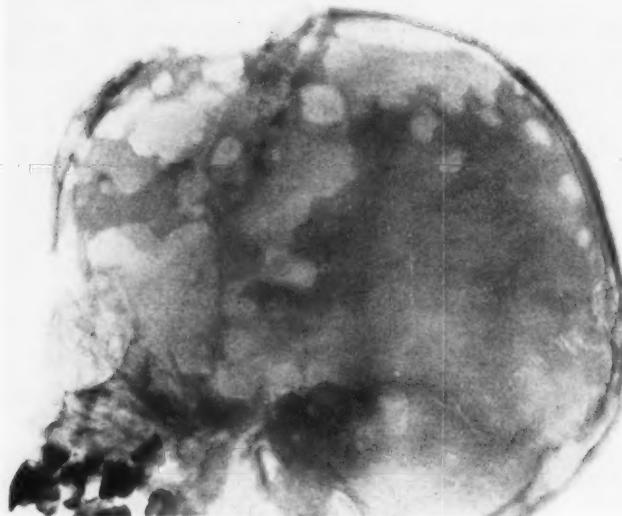


Fig. 183.—*x*-Ray of skull showing bone defects: lateral view.

The striking thing in a complete Roentgen ray study of the skeleton is the very extensive defects in the skull bones, slight but similar changes in the flat bones of the pelvis, and a quite normal appearance and normal stage of ossification and development of all other bones in the body. The defects in the skull caused an appearance which can be best described by comparing them to the irregular holes in a bit of moth-eaten flannel or the appearance of a pasteboard box gnawed full of holes by mice (Figs. 183, 184).

As seen in the lateral view (Fig. 183), the most extensive defects are in the anterior half of the skull. Of the frontal bone, particularly the lateral portions, only irregular rather narrow septa of bone are left between the large islands of entire bone disappearance. In a similar way the orbital plates of the



Fig. 184.—*x*-Ray of skull showing bone defects: frontal view.

frontal bone have largely disappeared, so that there is little bony support remaining for the eyeballs. In the parietal bones there are extensive defects in the vertex portions, whereas in the lateral portions of the parietal bones there are only a few round defects, measuring from 1 to 2 cm. in diameter. In the occipital bone only three small circular defects are present.

Viewed in the anteroposterior direction (Fig. 184) the very extensive defects in the frontal bones are very evident, as is also the irregularity in the orbits of the eye. The best idea of the character of the skull defects is obtained from stereoscopic plates, from which it is perfectly clear that the defects represent a complete loss of all bone substance capable of throwing any distinct shadow characteristic of bone. The variations in density at different places in the bones when seen in the ordinary plates are due to the fact that in some places there are defects on the two sides of the skull in line with each other, whereas in other places the defect on one side of the skull is opposite to a place where intact bone remains on the opposite side. Almost everywhere the margins of the defects are sharply cut, as if the line of demarcation between no bone and fairly normal bone is a very sharp one. Only here and there do the edges show a ragged appearance, indicating points where small projecting portions of bone remain intact. This picture may be due to the fact that the inner table at this point remains and the outer table has been dissolved or destroyed, or vice versa. At certain points in the stereoscopic plate it is evident that there are small round defects or cavities in the substance of the bone, with a thin inner and outer table still intact, and at one point in the lateral view the thin inner and outer tables can be seen projecting as faint shadows beyond the general substance of the bone. The character of the round defects of small size seems to be similar to the character of the large irregular defects. About none of these defects does the surrounding bone show any thickening or other evidence of proliferation, and where the defects do not exist the structure of the bone seems entirely normal. The sella turcica seems somewhat enlarged and slightly flattened, and in the stereoscopic view it looks as if there is a defect in the base of the skull very close to, if not continuous with, the sella turcica.

Plates taken at different times show very slight variations in the picture. On February 22, 1917, the defects were evidently less numerous and less extensive than on January 30, 1918. The last plates taken, those of June 10, 1918, after six months'

stay in the hospital and treatment with various forms of pituitary substance, show no change apparently of progression or retrogression in the defects as contrasted with the picture of January, 1918. All the other bones in the skeleton, except the pelvic bones, show no change whatever. In this bone in the lower half of the ilium there is slight irregular rarefaction suggesting small incomplete defects roughly circular in character, similar to what is seen in the skull, only very much less marked, and in the anterior portion of the ischium near the acetabulum there is also slight irregularity in the density, suggesting loss of substance.

#### DISCUSSION

A careful search of the literature revealed but one report of a similar condition. Schüller, in the *Fortschritte auf der Gebiete der Roentgenstrahlen*, 1915-16, xxiii, 12, under the title "Über eigenartige Schädeldefekte in Jugendalter," describes 2 cases observed by him in Vienna. In these,  $\alpha$ -rays of the skull show the same condition as described above in my case. His description is as follows:

CASE I.—"Boy of sixteen years, with normal family history. Except for measles the patient was well in the first years of childhood. He went through four classes in the Volksschule successfully. Since that time he has not grown any more. Three months ago the patient noticed that his left eye was more prominent than the right. Since then a slight inflammation of the left eye has been present. There has never been any headache, dizziness, vomiting, or decreased vision. Recently there has been double vision in looking to the side, affecting mostly distant objects. They stand either parallel or leaning toward each other. In January, 1913 the patient was 137.5 cm. high and weighed 39.5 kilos. Panniculus adiposus richly developed. Cheeks fat. On both sides of the neck above the clavicle are fatty tumors. Also in the thorax there is much fat and the abdomen is fatty. Arms and legs also are fatty. No abnormal findings in the internal organs. No symptoms of tuberculosis or syphilis. The genitals are small and completely infantile. The

right lobe of the thyroid is slightly larger than the left, but not abnormal. Skull dolichocephalic. Forehead is short and somewhat narrow. Over the left eyebrow the skull is somewhat sensitive. The face is asymmetric. The left half appears prominent and seems as if swollen. The left eye projects about 8 mm. beyond the right. Movements of the left eyeball unaffected. Nystagmus on looking to the side. In the fundus of the left eye the veins have dilated without pulsation. The fundus is normal.

"At different places in the Roentgen ray plate the left half of the skull shows clearing of the bone shadow corresponding to extensive ulceration of the skull. The greatest defect is in the region of the left parietal bone near the midline. This defect shows an irregular, nearly square form, diameter 3 to 5 cm. From the posterior lower corner of this defect goes a narrow horn-like, half-moon, curved process. The edges of the defect are sharp. The central part of the defect appears brighter than the periphery. Further defects are found in the region of the left frontal bone and in the region of the occiput. The walls of the left orbit do not appear changed as compared with the right. The sella is small. The dorsum sellæ is intact. Reflexes are normal. There can be no doubt that the combination of dystrophia adiposogenitalis and protrusion of the eye can be explained on the assumption of a tumor at the base of the brain. Other things suggest pressure. The suggestion is made that the tumor is an angioma of the dura or of the skull bone."

CASE II.—"Four-year-old girl who when one and a half years old had whooping-cough. When two years old she suddenly developed left-sided exophthalmos. At that time the physician who saw the child demonstrated a defect in the skull roof. Some months later a right-sided exophthalmos suddenly appeared. In October, 1913 the child was small and slender. Skin and mucous membranes were pale. Microscopic and Wassermann study of the blood was negative. Internal organs and neurologic examination was unimportant. There was no glandular swelling; no remains of any previous rickets. Intelli-

gence of the child seemed well developed. There were markedly increased thirst and polyuria, up to 8 liters daily. The child's head is of normal size and oval shape. The growth of hair is very sparse. Extensive portions of the scalp are free of hair. Both eyes show a high-grade exophthalmos. Vision amounts to at least 6/20. On both sides there is temporal pallor of the optic nerve. On palpation the skull shows several defects of different extent. They are partly oval, partly oblong. The edges of the defects are sharp and firm. Where the defects exist one feels the pulsations of the brain, but the membranous covering of the defect does not bulge, but seems slightly sunken.  $x$ -Ray of the skull shows very plainly the defects. They appear both in the transverse and sagittal picture as an entirely peculiar map-like spotting of the  $x$ -ray shadow. Only a relatively small part of the skull shadow corresponds to the normal bone thickness. Within very extensive regions one sees different sized and differently formed clear places. These are partly light gray and in part completely lack the ordinary darkening or shadow of bone. The former correspond to skull defects without any on the opposite side, so that, on the defect on one side, a bone shadow is projected from the opposite side. The latter are defects which overlie defects on the opposite side. The edges of the defects are completely sharp. When the defects appear in profile the edges have a funnel form, so that the defect in the lamina externa is greater than in the lamina interna. The skull between the defects seems entirely normal. Also in the region of the base of the skull extensive defects are recognized. The well-known contour of the upper edge of the orbit is completely lacking on both sides. The orbital roof appears almost completely eroded. The sella turcica is markedly changed. Only the dorsum sellae is present. The anterior part of the floor of the sella is greatly deepened. The destruction of the roof of the orbit explains the exophthalmos. In January, 1914 the symptoms had not changed. The defects in the skull plainly were smaller.  $x$ -Rays taken of the pelvis at this time showed a round defect about the size of a five-crown piece in the right ilium and also a spindle-like thickening in the upper part of the

right femur (healed fracture)." Reproductions of x-rays of the skull of this patient are almost identical with those of my patient.

Schüller goes on to say, "The explanation of this case is very difficult. The history makes it plain that it is not a congenital, but an acquired, disease of the skeleton. The clinical observation shows that the process is capable of regression. Most probably it is a primary bone disease in the sense of a system disease of the skeleton. One might think of a disturbance of the centers of ossification brought about through a disease of the glands of internal secretion. Diabetes insipidus occurs most frequently in affections of the hypophysis. The erosion of the sella turcica, demonstrable in the x-ray, might be caused by a tumor of the hypophysis region. The defects of the roof of the skull and of the ilium are, however, not explicable on the assumption of pressure from a hypophysis tumor. Experimental observations on the results of the extirpation of the hypophysis in young animals have shown that disturbance in bone development occurs in the sense of calcium poverty, so that the bones may show holes and suffer fractures. Also disturbance of the formation of the teeth could be brought into line with a disturbance in the hypophysis. We can make a presumptive diagnosis of anomaly of the skeleton as the result of disease of the hypophysis."

In some cases of muscular dystrophy, as pointed out by Janney and his co-workers (The Endocrine Origin of Muscular Dystrophy, Janney, Goodhart, and Isaacson, *Arch. of Int. Med.*, 1918, xxi, 185) and by others, atrophic changes occur in the skull bones somewhat similar to those found in my case and in the 2 cases of Schüller. In muscular dystrophy, however, the bone changes are by far less extensive. In their cases the following changes in the skull bones were noted. *Case II:* "The roentgenographic examination shows small spots of bone absorption scattered throughout the upper portion of the cranium." *Case III:* "The roentgenographic examination shows very marked bone rarefaction in the skull, evidently in the tabula interna, simulating strongly the convolutions of the brain."

*Case IV:* "Roentgenographic examination shows several small irregular spots of bone absorption scattered through the parietals and frontals." It is of particular interest that Janney and his associates are maintaining in this paper the thesis that muscular dystrophy is closely associated with disturbance in glands of internal secretion, and in one of their cases there was evidence of a causative connection between dyspituitarism and muscular dystrophy.

The only condition in which I have seen any resemblance to the bone picture of the case here reported, and that only a partial one, is multiple myeloma. With this condition the skull and other flat bones often show in the Roentgen ray scattered round or oval defects due to tumor growth. In these cases I have never seen any large irregular bone defects. In multiple myeloma palpation usually reveals a nodule where the Roentgen ray shows the larger bone defects, so the resemblance is but a superficial one.

Syphilis might cause somewhat similar bone defects from gumma formation. Schufeldt (Amer. Jour. of Syphilis, 1918, xi, 462) pictures a skull with most extensive destruction of bone from a negro of twenty-four, without further statement other than that "eventually the fact became known to me that this negro had died from tertiary syphilis." Adami and Nicholls (The Principles of Pathology, Lea & Febiger, Philadelphia, 1909, Vol. II, p. 1029, Figs. 289, 290) give a figure of a somewhat similar skull labeled "periostitis with destructive inflammation (osteoporosis) affecting the frontal and temporal bones supposedly due to syphilis." In syphilis, however, breaking down of the gumma and later scar formation in the scalp are to be expected. In my case no evidence exists of any previous local inflammatory condition, and the patient's blood Wassermann was negative.

Craniotabes in rickets occasionally shows thinning and defects in the skull bones, but there was nothing in our case suggestive of rickets. Osteoporosis congenita presents some similarity, but this is an ill-defined clinical group whose nature is too little understood to throw any light on this patient, and I

have found no cases described under this heading very similar to the case here reported.

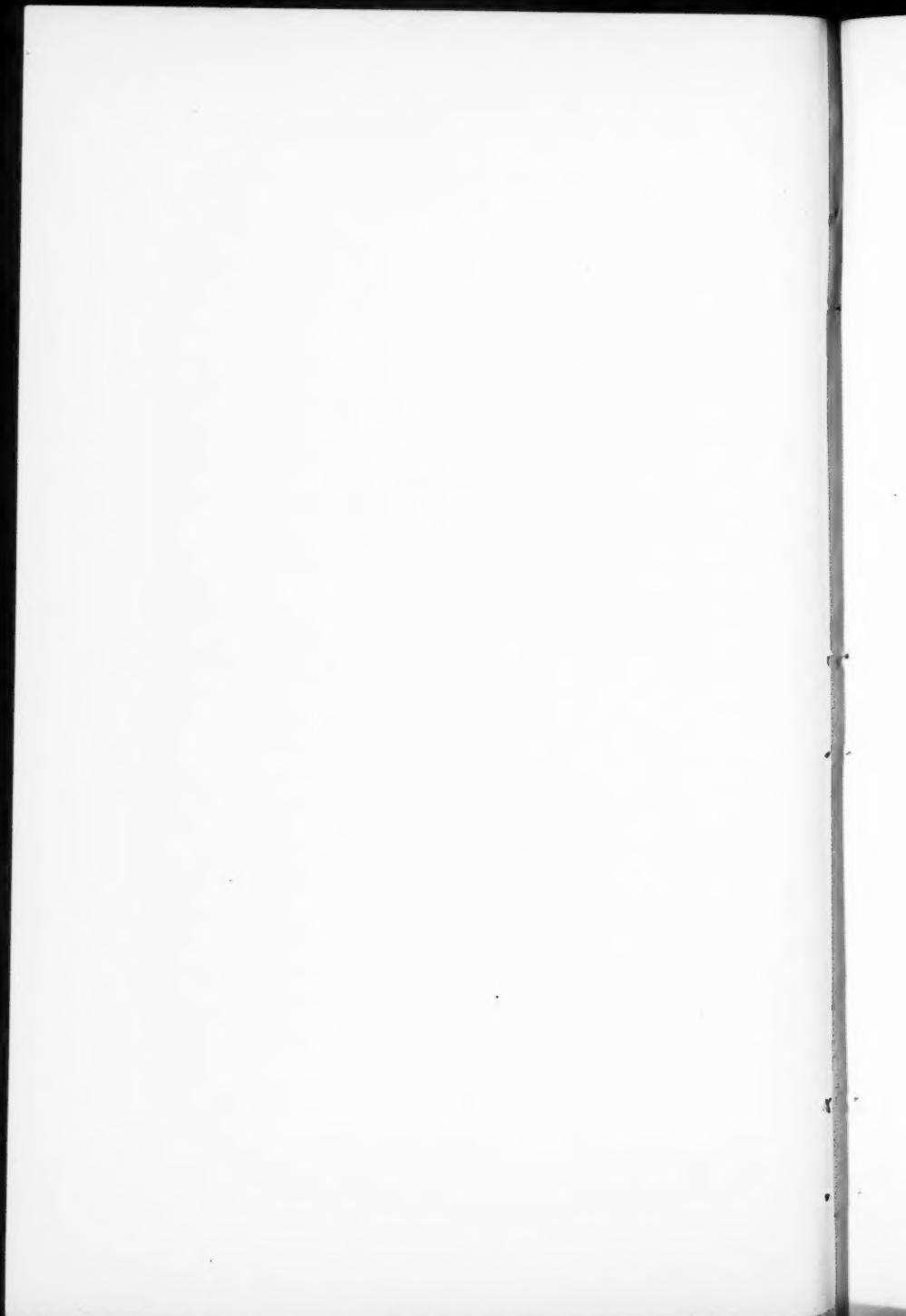
That a disturbance in the secretion of the pituitary gland is responsible for the defects in the flat bones in this case is a hypothesis that has considerable support. The coexistence of diabetes insipidus controlled by subcutaneous injections of pituitary substance is strong evidence of a disturbed pituitary function. Motzfeldt (Boston Med. and Surg. Jour., 1916, clxxiv, 644; Jour. Exp. Med., 1917, xxv, 153) and others have shown by clinical and experimental observations that there is a relation between diabetes insipidus and deficient pituitary function, as Motzfeldt expresses it, "lowered activity of the posterior lobe of the pituitary body." In the only 2 cases similar to mine that I can find reported (Schüller, loc. cit.) evidence of pituitary disturbance was noted, in one an adiposogenital dystrophy, in the other diabetes insipidus, as in my case. In such an unusual disturbance as is represented by the bony defects in these 3 cases it could hardly be a coincidence that there existed in each evidence of disturbance in the function of the pituitary gland. Rather does it seem highly probable that the bony defects are caused in some way by change in the pituitary gland, changes as to whose exact nature we have no evidence from the study of these cases.

#### **SUMMARY**

A case is presented where in a girl of five there occurred the symptom-complex of very extensive defects in the skull bones, exophthalmos, and diabetes insipidus. Only 2 other cases of this condition could be found in the literature. Diabetes insipidus suggests that the symptom-complex is due to a disturbance of pituitary function. Both of the other 2 reported cases showed evidence of disturbed pituitary function. In the case here reported pituitary extract controlled the polyuria when given subcutaneously. Other methods of introducing pituitary substance had no effect on the polyuria. No method of giving pituitary substance had any effect on the bone defects or the exophthalmos.

TABLE I

Date.	Volume of urine.	NaCl		Nitrogen	
		Per cent.	Grams.	Per cent.	Grams.
February					
7	6210	.03	1.86	.08	4.97
8	4885	.05	2.44	.05	2.44
9	7360	.03	2.21	.06	4.42
10	7260	.03	2.18	.06	4.36
11	7930	.01	.79	.04	3.17
12	8000+	.06	4.80	.05	4.00
13	6712	.02	1.34	.05	3.36
14		Two-hour renal test.			
15	5535	.04	2.21	.08	4.43
March					
22	1380	.13	1.79	.28	3.87
23	3556	.05	1.78	.12	4.27
24	2380	.13	3.09	.21	5.00
25	2670	.06	1.60	.17	4.54
26	2157	.11	2.37	.20	4.31
27	2382	.09	2.14	.14	3.33
28	1580	.14	2.21	.35	5.53
29	3050	.07	2.14	.15	4.58
30	3174+	.06	1.90+	.12	3.81+
31	4350	.07	3.05	.06	2.61
April					
1	2045	.15	3.07	.23	4.70
2	1961	.11	2.16	.25	4.90
3	2528	.15	3.79	.21	5.31
4	2268	.11	2.49	.23	5.22
5	2335	.11	2.57	.22	5.14
6	2025	.3	2.63	.20	4.05
7	4530	.06	2.72	.12	5.44
8	3215	.16	5.14	.23	7.39
9	2165	.17	3.68	.26	5.63
10	2412	.14	3.38	.24	5.79
11	3220	.12	3.86	.21	6.76
12	2551	.16	4.08	.20	5.10
13	3122+	.12	3.75+	.19	5.94
14	3445	.08	2.76	.20	6.89
15	3580	.08	2.86	.18	6.44
16	2495	.08	2.00	.17	4.24
17	3205	.08	2.56	.15	4.81
18	2068	.05	1.03	.22	4.55
19		Two-hour renal test.			



CLINIC OF DR. ELLIOTT P. JOSLIN

NEW ENGLAND DEACONESS HOSPITAL

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**DIABETES OF LONG DURATION  
SEVERE DIABETES VERSUS SEVERE ACIDOSIS IN  
DIABETES**

**DIABETES OF LONG DURATION**

THE oldest living college graduate always excites interest, though there is no especial rivalry among the alumni to succeed him. Similarly, among my diabetic alumni and alumnae there is no desire to usurp the place of my chronologically oldest living diabetic patient, though her freedom from symptoms of diabetes for nearly twenty years, and her survival of an operation for gall-stones at the end of this period, despite 0.3 per cent. albumin in the urine, might excite the envy of them all. In her case attacks of polydipsia, polyuria, and polyphagia developed at intervals of every four weeks at the age of thirty-five years in 1896. Systematic treatment was not carried out until 1900, when the patient became sugar free under the care of one of Naunyn's pupils and acquired a tolerance for approximately 100 grams of carbohydrate. Six months later I had the opportunity of seeing her for a few times, found the urine sugar free, the weight 135 pounds, which represented a loss of 35 pounds from her highest weight. She was, therefore, a mild case of diabetes associated with obesity, with onset in the fourth decade.

The average length of life of 88 fatal cases of diabetes with onset during the fourth decade, whom I have seen at one time or another, has been five years. This patient has already lived five times as long. It is true that her case was mild from the first and that she had exceptionally good treatment. However, few yet realize that these mild cases are the ones which give the greatest rewards for energetic care, but when neglected become

severe and constitute a reproach to the medical profession. The question now arises why this diabetic patient's span of life should have been extended so far and why she should hold pre-eminence in my series.

When a systematic search for the end-results of my patients was made in 1916, this patient came under my observation a second time. Upon that occasion the urine was free from sugar in the three specimens examined and albumin was present in but one. Casts were absent in all. The blood-sugar, fasting, was 0.09 per cent. The non-protein nitrogen was 19.6 mgm. per 100 c.c. On physical examination the blood-pressure was 125 mm. Hg. systolic and 90 mm. diastolic, and the only abnormality noted was a mass in the abdomen to be felt in the gall-bladder area. Through the assistance of Dr. Percy Brown this was demonstrated to be due to gall-stones.

At that time no operation was advised. How fraught with danger such a decision may be in the case of gall-stones the future course exemplified. But the patient was free from attacks, in fact, had had none for several years, and recalled these only with direct questioning. Furthermore, a diabetes of many years' duration had subsided, and it seemed more than desirable to leave well enough alone. Again an interval of several years intervened before another visit.

In the spring of 1919 the picture had changed, and instead of diabetes or gall-stones there was a marked nephritis. The urine contained 0.5 per cent. of albumin (Esbach test), with occasional casts. The non-protein nitrogen was 60 mm. per 100 c.c. A phenolphthalein test in May showed an excretion of 15 per cent. in two hours. The blood-sugar continued normal —0.09 per cent. Physical examination revealed an enlarged heart, a blood-pressure of 200 mm. systolic and 110 mm. diastolic, and failing vision. At what period the symptoms of renal trouble began to appear is not known, but an observation by a competent physician was on record which showed that the urine was certainly free from albumin in March, 1918. Between the following May and November, 1919, the albumin persisted in varying quantities, never being less than 0.2 per cent. Casts

were infrequent. However, the blood-pressure subsided to quite a degree, and occasionally would be as low as 150, but the eyesight grew worse. Later the non-protein nitrogen was 41. There was no estimation of the blood-sugar, but the blood-fat a few hours after a meal was 1.22 per cent.

Notwithstanding these various serious symptoms and signs the patient was quite comfortable and able to walk about in her garden until August, when she experienced an attack of severe pain in the upper abdomen, with tenderness over the gall-bladder accompanied by a temperature of 103° F., and jaundice. The attack soon subsided and the general condition of the patient again improved. Other attacks, however, recurred at frequent intervals, and, though not always as severe, they gradually reduced the patient's weight and strength. The condition of the urine did not particularly change. Finally, the urgency of the situation forced a decision as to whether this patient, who had once had diabetes, who showed severe Bright's disease with a blood-pressure at times nearing 200, and with an excretory power for phenolphthalein of 15 per cent. in two hours, would survive an operation. At length, all agreed that there was quite as much safety in boldly operating as in temporizing. Consequently the patient went to the hospital and a laparotomy was performed by F. B. Lund. Gall-stones were evacuated from both the gall-bladder and common duct and the gall-bladder drained. As not so seldom happens, the patient who had been in a desperate condition and a most unfavorable operative risk, did exceptionally well. Sugar appeared in the urine to the extent of a few tenths per cent. following the operation, but convalescence was uninterrupted, and twenty days after entering the hospital she was discharged and has steadily improved. Now, two months after the date of operation, the urine contains less albumin than at any time since the spring, and sugar has been absent save immediately following the operation. The patient has regained some of the weight lost and is better in every way than for months.

You will agree with me, I am sure, that my oldest living diabetic patient teaches many lessons.

First of all, did the patient actually have diabetes? No question of its existence was felt in 1900, and a definite test of the carbohydrate tolerance was made and this was considered to be equivalent to 120 grams of bread. There seems to be no valid reason to doubt its presence.

Long life and diabetes are compatible; 34 of my patients have outlived the standard tables for the expectation of life for their age at the onset of their disease. In seeking for a cause for diabetic longevity the age of the individual is of first importance. The following table of duration of my fatal and living cases, seen prior to February, 1918, shows that the disease during the first two decades is of the shortest duration, next in the third decade, but subsequently varies little. The somewhat shorter duration of life of patients who develop diabetes in the seventh and eighth decades is hardly more than is to be expected on account of advanced years.

DURATION OF FATAL AND LIVING CASES OF DIABETES BY DECADE OF ONSET

Age of onset. Years.	Fatal.		Living.	
	No. of cases.	1893 to 1919 Duration, years.	No. of cases.	1893 to 1919 Duration, years.
0-10 . . . . .	53	2.5	15	4.7
11-20 . . . . .	81	2.8	23	4.6
21-30 . . . . .	79	3.5	51	8.2
31-40 . . . . .	88	5.0	80	8.3
41-50 . . . . .	138	7.2	158	8.3
51-60 . . . . .	164	7.2	112	6.9
61-70 . . . . .	89	6.0	32	7.6
71-80 . . . . .	27	4.1	9	6.1
81-90 . . . . .	1	2.9	—	—
Totals. . . . .	720	5.4	480	7.6

Age may not be quite so decisive a factor as has hitherto been supposed, but before reaching such a conclusion all causes of death not directly attributable to diabetes ought, perhaps, to be excluded. A second and favorable factor is obesity; a third, the favorable environment of the patient; a fourth, the careful treatment in the first years; a fifth, an intelligent patient, for,

say what one will, this counts for a very great deal. Diabetic patients who live long are rather superior individuals, and although they may boast they have not lived on a diet, upon questioning them closely one finds either that the total diet has been limited or that the quantity of carbohydrate has been markedly reduced. For example, 2 of my most notable cases eat but two meals a day. Sixth, and finally in this case, the possible etiologic factor of gall-stones.

The association of diabetes and gall-stones naturally is not uncommon, because both diseases are prone to occur in the latter half of life. As a rule, gall-stones precede diabetes, but I have met with one striking instance in which diabetes occurred following an operation for gall-stones, and F. C. Brigham has told me of another. It will not be long before one of you students will perform sugar tolerance tests upon all the gall-stone patients in the hospital in order to discover latent diabetes. In my case a fat man, following an operation for gall-stones at a time of great business worries, was given a considerable quantity of candy. Sugar, which was absent before the operation, reached 7.2 per cent. one month later, but subsided with careful dieting. The average age of onset of the gall-stones in 18 of my own diabetic cases was forty-three years, but the average age of onset of diabetes in the same individuals was forty-nine years. Statistics and circumstances like these just mentioned furnish an argument in favor of an early operation for gall-stones in diabetic patients. Whether the diagnosis of gall-stones in the diabetic should invariably indicate their removal is still somewhat of a question. Years ago one would have answered unhesitatingly "No," but at the present moment, with an expert surgeon and favorable conditions for surgical and medical care, I am advising one of my patients who presents this condition to have the operation, although neither the diabetes nor the symptoms from gall-stones are severe.

The operation for the removal of gall-stones in the diabetic can be carried out successfully provided there is intimate co-operation between physician and surgeon. Naturally, one would choose for the time of operation an interval between attacks and

would arrange that the patient be free both from sugar and evidences of acid poisoning as well. However, if an emergency exists, an operation can be done even in the presence of sugar. Do not fast a patient or change the diet in an extreme manner preceding an emergency operation save to omit the fat and to give the carbohydrate and protein in the simplest forms of food. Following the operation continue the diet as before, taking the greatest pains to avoid any article of food which will cause indigestion. So often diabetic patients are given coarse vegetables in their regular diet that, unless one is cautious, these will creep into the food prescribed for these same cases both before and after operative interference. The results of such an error are often unfortunate.

The operation should be performed swiftly and with no unnecessary trauma, and it demands a surgeon who has the fabled skill of the old French school. Ether and chloroform should be avoided and gas-oxygen employed. It is true that at some clinics ether is still used in operations upon diabetics, but I think the patients of the most notable of these clinics, which cling to ether, survive in spite of ether rather than because of it, and in my opinion the favorable results reported have been probably due to two facts, first, that actually very little ether has been employed, and, second, that the operative technic has been of the highest quality.

It is quite possible that following the operation the sugar may return in the urine for a day or two, or, if it has previously existed, may increase. This need cause no anxiety and indicates no need of deviation from the well-thought-out plan of diet. Little by little the sugar can be eradicated.

Patients with nephritis and, in fact, patients showing high blood-pressures are by no means always so fortunate as was this patient when they submit to surgical interference. Not long ago another patient of similar character after an operation of necessity developed hemiplegia. You shold not conclude that such cases are to be operated upon thoughtlessly. Only when the chances of surgical interference are better than the chances of non-interference is one justified in calling the surgeon. Cour-

age, however, is a great virtue, and one should ever have it with him in treating diabetic patients.

The second patient with diabetes, whom I would now present to you on account of the long duration of his disease, developed definite symptoms in 1898 at the age of forty-seven years. Of him I would say that no patient with diabetes has been seen by me in the last eight months who has appeared for his age in as robust a condition as this man. With his history of twenty-one years of diabetes he teaches us all several lessons. First of all, he weighs 230 pounds. His highest weight was 260 in 1911, and his lowest since onset 216 pounds in 1918, and his weight at onset was 200 pounds. When he came to the office I could hardly resist telling him that he was visiting the wrong doctor and frankly confessed that I expected to learn more from his story than he could gain from my treatment. He tells me that for the last fifteen years he has constantly shown sugar in the urine. With our established rules of strict dieting we should all bear this in mind. It is of importance. Although the patients who are sugar free and the patients who have a normal blood-sugar appear to do the best, here is a man who has had sugar in the urine for fifteen years and is in good condition. His blood-pressure at nearly sixty-nine, after twenty-one years of diabetes, is 170 mm. systolic and 80 mm. diastolic. His heart, lungs, liver, spleen, and kidneys are normal. In particular there is no albumin in the urine. The non-protein nitrogen in the blood was 25 mgm. per 100 c.c. A Wassermann reaction was negative. The phenolphthalein test was 38 per cent. in two hours. The quantity of sugar in the urine is 2.5 per cent. Diacetic acid is absent. The duration of the case and the persistent presence of sugar in the urine are not the only features. This gentleman's blood-sugar is 0.200 per cent., fasting. After his noon meal it rose to 0.250 per cent. Presumably the blood-sugar has been high for a decade, and yet the man presents a remarkably healthy appearance. We would all do wrong if we did not seriously consider this fact and attempt to explain it. This gentleman, like the former patient, has had the unusual opportunity of being able to take care of himself. His disposi-

tion is serene, he has exercised continuously throughout this entire period, has retired from business, and has had few worries. His diabetes, too, was obviously mild at the start. I must acknowledge that he could hardly be in a better condition today if he had been kept sugar free these fifteen years. But upon questioning him I find that he has at no time during this entire period been careless about his diet. His carbohydrates have always been reduced. He has not eaten white bread, and although the bread he has taken has contained a considerable quantity of carbohydrate, it was not always easy for him to get it, and so the quantity of even this substitute bread was restricted. This is one incidental advantage of so-called diabetic foods, and may explain why they sometimes work well, just as the old doctors often obtained good results in the treatment of gout by limiting their patients to white meat.

I confess that though this man has done well, when I allow one of my patients to show sugar constantly, it is almost an invariable rule for the individual to grow rapidly worse. Elderly diabetics must not be neglected. It should be remembered that it is rare to see a case of gangrene in a diabetic, though of advanced years, if the urine is sugar free.

#### SEVERE ACIDOSIS IN DIABETES VERSUS SEVERE DIABETES

Two cases of severe acidosis in diabetes have been exquisitely reported; the one by Geyelin and DuBois (Jour. Amer. Med. Assoc., 1916, lxvi, p. 1532. Also, Gephart, Ault, DuBois and Lusk, Arch. Int. Med., 1917, xix, p. 908) and the other by Fitz and Bock (Amer. Jour. Med., 1919, vol. xii, No. 48). These patients, who represent two of the severest instances of acidosis with recovery on record, later acquired a tolerance for carbohydrate of 110 grams (2639 calories) and 150 grams respectively. One case, however, died subsequently in the course of six months, but the fate of the other I do not know. The encouraging feature about these cases to me is the fact that although the authors concluded that these patients were of the severe type of diabetes, basing their decision upon all the criteria at their command, including the dextrose-nitrogen ratio, yet when the attack

of acidosis was over the cases could plainly not be classed as of the severe type of diabetes at all, but rather as cases of moderate severity. Their acidosis was severe but incidental, and very likely avoidable. The fact that severe acidosis occurs in diabetes which is not severe is not sufficiently recognized. It is a very important fact, because unless you gentlemen realize that your patient approaching coma may not, after all, be a severe case of diabetes, you will lose heart in your treatment. In former days the cases of diabetes succumbing to coma soon after entrance to the hospital were, to a large extent, only moderately severe or even mild cases of diabetes with severe acidosis, rather than cases of severe diabetes with acidosis. This is perfectly obvious if you look at the duration of life of the fatal cases of diabetes occurring in hospitals in former years. You will find that upward of 67 per cent. of the fatal cases occurred during the first year of the existence of diabetes, in contrast to 12 per cent. of cases treated more recently and in private practice.

May I now call to your attention another case in my series which to me is of especial interest, because hitherto no patient with acidosis of greater intensity than his has been admitted to the Corey Hill or Deaconess Hospitals and later departed alive. In this instance I believe all would admit that the severity of the disease following recovery from the attack of acidosis was greater than that of the 2 patients so admirably reported by the authors mentioned. This man developed diabetes at the age of thirty-nine years in 1913. Since that date his weight has fallen from 184 to approximately 130 pounds. On June 30, 1919 his physician telephoned to me that he was in beginning coma and asked that he be admitted to the New England Deaconess Hospital. Upon arrival he was breathing deeply, the skin was dry and flushed, the pulse 100. There was an acetone odor to the breath, slight edema of both ankles, a very favorable symptom in my experience when coma is impending. The urine showed acetone and diacetic acid 4+, sugar 3 per cent. The  $\text{CO}_2$  in the blood in terms of mm. Hg. for comparison with  $\text{CO}_2$  in the alveolar air was 12.8. The  $\text{CO}_2$  in the aveolar air was 12 mm. Hg. The Wishart acetone test in the blood was positive.

You may be very sure that physicians and nurses were alert when this patient arrived, and the following treatment was instantly instituted: (1) The patient was placed in bed and his strength thus conserved. He was made comfortable, anxiety allayed. (2) Care was taken to keep the patient warm. It was not necessary to apply heaters, although in cold weather it is easy for a patient to become uncovered and to lose heat from restlessness and exposure. This is one of the chief reasons for allaying nervousness and providing against discomfort. In a recent case  $\frac{1}{16}$  grain of morphin quite sufficed to obviate the pain which a patient experienced in back and chest. A very small dose of morphin or codein is adequate in diabetic coma. (3) A special nurse was provided for the patient both for day and night, and pains were taken to secure a nurse with a diabetic experience. Indeed, every possible means must be employed to bring victory in such a life-and-death struggle as is the contest between the doctor and diabetic coma. (4) The bowels were moved by enema, so that later salt solution could be given by rectum if required. Cathartics were purposely avoided in order to obviate diarrhea, which might render the rectum intolerant. (5) The tolerance of the stomach for liquids was conserved. Therefore, hot liquids amounting to 1000 c.c. were administered during every six hours. Care was taken to give these slowly, so as to avoid upsetting the stomach. In consequence, it was unnecessary to give any of this liquid by rectum. It is often desirable to administer a portion of the same in the latter manner, because this protects the stomach, and it is advantageous to do this too soon than too late. In case difficulty is experienced in giving 1000 c.c. in six hours, the salt solution can be given intravenously or even subpectorally.

(It may not be amiss to digress to call your attention to a possibility of treatment new to me. This came from observation of a recent case of A. L. Chute, to whom salt solution was given subpectorally many times. Dr. Chute's patient had cancer of the penis and diabetes of twenty-two years' duration. The urine contained 3.4 per cent. sugar without acidosis. Prior to the operation, which consisted of total extirpation of the genitals,

he was made sugar free, and he has remained practically sugar free since upon a diet of carbohydrate 74 grams, protein 65 grams, and fat 52 grams. Often, as with this case, the reduction of calories serves to increase the tolerance in the course of weeks far above the tolerance which was originally found. These patients are very instructive, for there is no danger of voluntary lapses in diet. Difficulties were encountered in the administration of liquids soon after the operation because the patient was temporarily irrational. Therefore he was given subsequent to the operation twenty-three subpectoral injections of salt solution, each amounting to 750 c.c. During this period the blood-sugar of this individual remained close to 0.263.

The harmlessness of these subpectoral injections confirms Allen's similar experience with diabetic dogs. It would appear as if trouble with subcutaneous injections arose formerly from two factors: (1) Improper technic, and (2) the introduction of sodium bicarbonate in conjunction with the normal salt solution.)

Empirically advances are often made in medicine, and perhaps the success obtained in the administration of warm liquids is partly due to the circumstance that warm liquids consist of broths, and these contain salt. If you will consult the old records which show recoveries from diabetic coma you will observe that these individuals not only voided large quantities of urine, often 8000 c.c. or more, but that the quantity of salt in the urine was low, perhaps indicating the body's need for it or lack of it. The taste of the patient, too, must be borne in mind and variety in the form of liquids must be secured.

The result of these measures was gratifying. The chart on p. 884 shows the gradual disappearance of acidosis and the acquirement of a tolerance for carbohydrate of 26 grams when the calories were nearly 20 per kilogram body weight. He was among the early cases treated after returning from service in the army, and today I should desire to bring the blood-sugar to normal by feeding protein alone for one or two weeks and then bringing the calories up to a livable ration. The general plan of treatment which usually followed has changed gradually, but is summarized on the cards shown on pages 885 and 886. The

## SEVERE ACIDOSIS IN SEVERE DIABETES

Date.	Urine.			Diet in grams.			Blood.			Alveolar air CO <sub>2</sub> mm. Hg.
	Vol. c.c.	Diacetic acid.	Nitrogen, grams.	Ammonia, grams.	Total sugar, grams.	Carbohydrate.	Protein.	Fat.	Calories.	
1919										
June 30	...	+++	...	...	(3.0%)	...	...	...	...	12.8
July 1	3450	++++	...	3.4	145	66	6	288	0.81	0.282
2	3160	++++	19	3.7	126	66	6	288	...	...
3	3180	++	20	3.2	70	66	6	288	1.04	0.217
4	3610	+	16	3.8	101	40	5	2	198	...
5	2920	+	15	2.3	58	40	5	2	198	...
6	1920	+	...	2.6	25	0	0	0	0	25
7	2420	+	...	2.2	24	0	0	0	0	29
8	2770	0	...	2.3	15	0	0	0	0	24
9	2280	++	...	2.5	18	0	0	0	0	...
10	2120	++	...	...	13	20	29	0	196	26
11	2000	++	...	2.0	34	20	45	10	350	...
12	2400	++	...	3.8	89	20	45	10	350	18
13	2480	+	...	1.1	17	20	10	4	156	...
14	2000	+	...	1.5	28	20	10	4	156	...
15	2000	+	...	0.8	6	15	8	3	119	1.11
16	1620	0	...	1.2	3	0	0	0	0	24
17	2050	0	...	0.7	1	0	0	0	0	...
18	2400	0	...	...	0	2	15	9	149	...
19	1624	0	...	...	0	4	22	14	230	...
20	1865	0	...	...	0	6	39	18	342	29
20	1865	0	...	...	0	8	48	24	440	0.56
22	1240	0	...	...	0	9	61	24	496	...
24	1878	0	...	...	0	0	0	0	0	...
25	2010	0	...	...	0	8	38	22	382	...
26	1890	0	...	...	0	10	51	22	442	...
28	1160	0	...	...	0	14	60	29	557	...
29	1420	0	...	...	0	16	64	38	662	0.198
31	1800	0	...	...	0	0	0	0	0	...
Aug. 1	1960	0	...	...	0	10	57	22	466	...
2	2000	0	...	...	0	11	64	28	552	...
3	2200	0	...	...	0	14	65	29	577	...
4	1800	0	...	...	0	15	69	38	678	...
5	1200	0	...	...	0	18	73	46	778	0.200
7	1800	0	...	...	0	0	0	0	0	...
9	2000	0	...	...	0	15	69	38	678	...
10	1900	0	...	...	0	18	73	46	778	...
12	1700	0	...	...	0	21	78	51	855	0.200
18	1500	0	...	...	0	24	79	66	1006	...
20	1800	0	...	...	0	26	80	71	1063	...
21	2000	0	...	...	0	10	39	16	340	...
22	...	...	...	...	...	...	...	...	0.182	...

patient returns to the hospital each month for the estimation of blood-sugar. I regret to say that this has increased and is now 0.218. He should re-enter the hospital now, voluntarily, rather than wait some weeks until forced to do so. He illustrates the need of continued medical attention in the home, and that, gentlemen, is your golden opportunity.

**Preparation for Fasting.** In severe, long-standing, complicated, obese, and elderly cases, as well as in all cases with acidosis, or in any case if desired, without otherwise changing habits or diet, omit fat, after two days decrease protein, and halve the carbohydrates daily until the patient is taking 30 grams or less; then fast. In other cases begin fasting at once.

**Fasting.** Fast four days, unless earlier sugar-free. Allow water freely, tea, coffee, and thin clear meat broths as desired.

**Intermittent Fasting.** If glycosuria persists at the end of four days, give 1 gram protein or 0.5 gram carbohydrate per kilogram body weight for two days, and then fast again for three days unless earlier sugar-free. If glycosuria remains, repeat and then fast for one or two days as necessary. If there is still sugar, give protein as before for four days, then fast one, and then gradually increase the periods of feeding, one day each time, until fasting one day each week.

**Carbohydrate Tolerance.** When the twenty-four-hour urine is free from sugar give 5 or 10 grams carbohydrate (150 to 300 grams of 5 per cent. vegetables) and continue to add 5 or 10 grams carbohydrate daily (more in mild cases) up to 50 grams or more until sugar appears, then fast until sugar free.

**Protein Tolerance.** When the urine is again sugar-free decrease the carbohydrate by one third below the carbohydrate tolerance or at least 10 grams, and then add about 20 grams protein and thereafter 15 grams daily in the form of egg-white, fish or lean meat (chicken) until the patient is receiving from 1 gram to 1.5 grams protein per kilogram body weight.

**Fat Tolerance.** It is usually desirable, especially in the young, to add no fat until the protein reaches 1 gram to 1.5 grams per kilogram body weight and the blood sugar is normal. Then add 5 to 25 grams daily, according to previous acidosis until the patient ceases to lose weight or receives in the total diet 20 to 30 calories per kilogram body weight.

**Reappearance of Sugar.** The return of sugar demands fasting for twenty-four hours, or until sugar-free. Resume the former diet adding fat gradually and last of all in order to maintain as high a carbohydrate tolerance as possible, sacrificing body weight for this purpose.

**Weekly Fast Days.** Whenever the tolerance is less than 20 grams carbohydrate, fasting should be practised one day in seven; when the tolerance is over 20 grams of carbohydrate cut the diet in half on one day each week.

The foods commonly employed in determining the tolerance for carbohydrate and protein are 5% vegetables, oranges or grape fruit, oatmeal or shredded wheat, potato, fish, chicken, lean meat, skimmed milk.

**Water, clear broths, coffee, tea, cocoa shells and cracked cocoa can be taken without allowance for food content.**  
**FOODS ARRANGED APPROXIMATELY ACCORDING TO CONTENT OF CARBOHYDRATES.**

	5%	10%	15%	20%
VEGETABLES (fresh or canned)				
Lettuce	Tomatoes	Str. Beans	Green Peas	Potatoes
Cucumbers	Brussels	Pumpkin	Artichokes	Shell Beans
Spinach	Sprouts	Turnip	Parsnips	Baked Beans
Asparagus	Water Cress	Kohl-Rabi	Canned	Green Corn
Rhubarb	Sea Kale	Squash	Lima Beans	Boiled Rice
Endive	Okra	Beets		Boiled Macaroni
Marrow	Cauliflower	Carrots		
Sorrel	Egg Plant	Onions		
Sauerkraut	Cabbage	Green Peas		
Beet Greens	Radishes	canned		
Dandelion	Leeks			
Greens	String Beans			
Swiss Chard	canned			
Celery	Broccoli			
Mushrooms	Artichokes			
Ripe Olives (20% fat)		Watermel'n	Raspberries	Plums
Grape Fruit		Strawberr's	Currents	Bananas
		Lemons	Apricots	Prunes
FRUITS		Cranberries	Pears	
		Peaches	Apples	
		Pineapple	Huckleberr's	
		Blackberr's	Blueberries	
		Gooseberr's	Cherries	
		Oranges		
Nuts	Butternuts	Brazil Nuts	Almonds	Peanuts
	Pignolias	Bk Walnuts	Wal'ts(Eng.)	
Musc.	Clams	Hickory	Beechnuts	40%
	Oysters	Pecans	Pistachios	
	Scallops	Filberts	Pine Nuts	Chestnuts
	Liver			
	Fish Roe			
* Reckon carb. in veg. of 5% group as 3%—of 10% group as 6%				
(30 grams 1 oz.)				
CARBOHYDRATES				
CONTAIN APPROXIMATELY				
G. G. G.				
Oatmeal, dry wgt.	20.	5.	.2	120
Shredded Wheat	23.	3.	.0	104
Cream, 40%	1	1	12	120
" 20%	1.	1.	.6	60
Milk	1.5	1	1	20
Brazil Nuts	2.	5.	20	210
Oysters, six	4	6	1	50
Meat (uncooked, lean)	0.	6	3	60
" (cooked, lean)	0	8	5	75
Bacon	0.	5.	15	155
Cheese	0.	8.	11	135
Egg (one)	0	6	6	75
Vegetables 5% group	1.	0.5	0	6
Vegetables 10% group	2	0.5	0	10
Potato	6	1	0	30
Bread	18.	3.	0	90
Butter	0	0	.25	225
Oil	0	0	.30	270
Fish, cod, haddock (cooked)	0.	6.	0	25
Broth	0	0.7	0	3
Fruit 10%	3.	0	0	12

## CLINIC OF DR. WILLIAM H. ROBEY, JR.

CITY HOSPITAL

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### PERICARDITIS

#### Leading Points in Diagnosis. Treatment and Management.

PERICARDITIS may be fibrinous, serous, purulent, or adherent. In dealing with any acute infectious or chronic disease the physician should have always in mind the possibility of its occurrence. If it is in mind and consequently searched for, it is less likely to be overlooked. Osler said some years ago that pericarditis is most frequently found in the autopsy room, but refinements in physical diagnosis are making it more apparent during life.

In the course of the acute infectious diseases, especially acute arthritis, fibrinous pericarditis may appear and should be constantly looked for, because a fibrinous pericarditis, although it may be accompanied by an amount of exudate sufficient to cause only slight, if any, changes in the cardiac outline, generally means a probable endocarditis, for it must be remembered that endocarditis, myocarditis, and pericarditis often go hand in hand. The prognosis in such cases should be guarded, since endocarditis may not be evident for several years after the infection. This is especially true of mitral stenosis and aortic regurgitation.

In a pericarditis which remains dry or, rather, has but a moderate increase in fluid, the sole physical sign is the to-and-fro friction-rub. It is generally heard, if only for a few hours, in almost every case of plastic pericarditis, and by systematic examination it will be found. Some authors state that when once distinctly heard it can scarcely be confounded with anything else, but the writer's experience with colleagues and graduate students points to the difficulty in distinguishing the

rub from valve murmurs. The rub even when faint will generally have a jerky, grinding, or leathery quality. Because of the more active movements of systole it may seem to be wholly a systolic sound, but by listening carefully one of similar quality, sometimes very faint, will be heard in diastole.

When the rub disappears it may mean that the fibrinous pericarditis has subsided, or that sufficient fluid has accumulated to separate the pericardial surfaces. The relative signs of fibrinous and serous pericarditis can best be discussed by a recital of cases.

B. G., white, housewife, age twenty-nine years, born in Pennsylvania, entered the hospital on April 9th. The patient did her housework, which was quite arduous, and continued at her duties until one week before entrance. She had been married twelve years, having had three healthy children and three miscarriages, which occurred between the second and third healthy children. The miscarriages came in each instance at the end of the third month. She had never been strong. As a small child she had measles, mumps, pertussis, scarlatina, and diphtheria; and at the age of sixteen there was an attack of rheumatic fever, with swollen, hot, tender, reddened joints. Three years ago there was a second attack similar to the first. Eight months ago she had influenza without complications. She suffered from headaches, worse in the morning and disappearing about noon. There were frequent fainting spells at the time of menstruation. During the past week there had been cough, worse at night and unrelieved by cough mixtures. She has been sleeping on three or four pillows to relieve the cough. There had been edema of the feet for the last three years, much increased recently. Her present illness began with hemoptysis (bright red blood), precordial pain, palpitation, and extreme dyspnea on exertion. On climbing stairs she had to sit down and rest. There were night-sweats for a month before entrance. The appetite had been poor, and since the beginning of the present illness there had been nausea and vomiting. She has never had hemorrhoids or bloody stools. The menstruation began at fourteen and has always been regular without menorrhagia.

or metrorrhagia. She drank 3 cups of tea and 3 of coffee daily. Her best weight was 130 twelve years ago, and 98 six months ago.

Five days before entrance she had severe palpitation and dyspnea on exertion. She went to bed, was feverish, had a chill, headache, conjunctivitis, and coryza. The following day she awoke with nausea, vomiting, and severe precordial pain. Her cough produced bright yellow sputum, but no blood. The dyspnea became quite severe even when lying in bed.

The examination at entrance showed a moderately well-developed but poorly nourished woman lying propped up in bed, with labored breathing and the appearance of considerable suffering. The head examination disclosed an injected throat, small buried tonsils, and an almost complete dental wreck. The precordia was slightly prominent. The right cardiac border was 5 cm. and the left 15 cm. from midsternum. The cardiac impulse was in the fifth space, in the nipple line, the area of cardiac dulness extending outside the impulse 4 cm. A loud grating to-and-fro friction-rub was heard over the entire precordia.

Over the base of the left lung there was dulness up to the angle of the scapula, with increased tactile and vocal fremitus, bronchial breathing, and increased spoken voice.

The temperature at entrance was 100.4° F., and rose the following evening to 102.6° F., but in three days fell, and throughout her illness ranged between normal and 100° F.

The pulse was never high, being between 80 and 90 throughout. The respirations were 35 at entrance, and varied from 25 to 30 during the entire course. The blood-pressure was: systolic 128, diastolic 52; pulse pressure 76. The white count at entrance was 7200, and ten days later 9400.

Here we see a young woman, never strong, never able to get much rest or change from household duties, with a history of several previous acute infections, especially two attacks of moderately severe acute arthritis. Her small buried tonsils, and particularly her very carious teeth, would have been foci of infection of joints and heart. Her dyspnea, cough, hemoptysis, and loss of weight focused our attention on the chest. The mod-

erate fever, relatively low pulse, and normal white count led us to negative an acute pulmonary infection notwithstanding the signs of consolidation in the left back. The dyspnea and orthopnea, the bulging precordia, the enlarged cardiac area, the to-and-fro friction sound, and the precordial pain, all suggested an acute pericarditis superimposed upon a chronic heart.

Examinations of the sputum failed to show the presence of tubercle bacilli. Her night-sweats, loss of weight, and hemoptysis, with signs of consolidation at the left base, made us feel the necessity of ruling out this condition. It must be remembered, however, that pericarditis is almost always a very late complication of tuberculosis. In twenty years I recall but one case—a woman whose lungs were filled with tuberculous foci.

On April 13th the cardiohepatic angle was found to be obtuse. With the presence of a to-and-fro friction-rub over the precordia at entrance this angle was constantly under observation because it is the area where fluid is most apt to accumulate. In the normal heart percussion gives practically a right angle where the right border of cardiac dulness joins the line of hepatic flatness. In cardiac hypertrophy or dilatation the right border often curves inward where it meets the hepatic flatness, but when the fluid is collecting the angle is, in many cases, obtuse. In the x-ray plate taken on April 12th the right border was  $7\frac{1}{2}$  cm. from midsternum and the left  $13\frac{1}{2}$  cm. On May 3d the right border was  $9\frac{1}{2}$  cm. and the left 12.9 cm. The heart picture showed the "bottle shape" which is seen in a certain number of cases of pericardial effusion. The x-ray was not materially helpful. Aspiration was done as a diagnostic procedure because of persistent dyspnea and cyanosis.

In purulent pericarditis, however, where the accumulation of pus is small or encapsulated, the cardiohepatic angle may not be altered. This was shown in x-ray plates recently exhibited by Major W. J. Stone. Where the fluid (serous or purulent) is largely posterior the angle may not be changed and the cardiac impulse will remain prominent.

Under salicylates the patient seemed to improve for a few days. It is important to remember that in serous effusions,

since they are often the accompaniment of acute arthritis, the salicylates act beneficially and sometimes very promptly. One of my colleagues was called in consultation to see a case of pericarditis with marked dyspnea and cyanosis. The man was in extremis, but because the attending physician's aspirating set was faulty and the patient being in the country, aspiration was delayed until the following day. The illness had begun one week before with a sore throat, and, acting on this etiology, the consultant ordered large doses of salicylate of soda, and returning the next day found the patient so much improved that aspiration did not seem necessary.

On April 19th the temperature became normal and the pulse 76. The pain in the cardiac area was present, but less intense and the general condition slightly improved. The extreme dulness in the left back about the angle of the scapula persisted, with bronchial breathing and egophony. The right border of the heart was 7 cm. from midsternum and the cardiohepatic angle obtuse. The to-and-fro rub was limited to the sternal area and over the apex impulse a systolic blowing murmur was heard. On the 27th the pain became more marked, but less intense than at entrance. The rub appeared once more over the entire precordia, the right border had diminished to 5 cm. from midsternum. During four days there were pain and tenderness in the left knee. There was slight edema of the feet and ankles.

On the 29th considerable cough developed, with thick, mucopurulent, occasionally blood-streaked sputum. The pain in the chest became much less. On the cessation of pain, notwithstanding the fact that the cardiac area to percussion had grown less, the possibility of an effusion largely posterior to the heart as evidenced by a probable Ewart's sign in the back, indicated aspiration of the pericardial sac. A needle was introduced through the fourth space, just to the right of the sternum. The needle was introduced slowly, the skin about the area having been thoroughly cocainized. We have not been in the habit of incising the skin as Pendlebury suggests. It is a good plan to have a window in the tube connected with the needle so that

the first passage of fluid may be observed and the further introduction of the needle stopped. It is the opinion of the author and many others that even if the point of the needle enters slightly into the cardiac muscle no harm is done. Indeed, in a case of firmly adherent pericardium such as the above case proved to be, it would be almost impossible not to slightly wound the heart muscle. There was no change in the patient's condition after aspiration. Aside from the moderate discomfort caused by the introduction of the needle, there was no difference. The chart showed no alteration either in pulse or temperature. It must be remembered that the pericardial space is potential, and if any fluid is withdrawn, it means an increase above the normal. No fluid was obtained. Although the left back now showed flatness below the eighth rib and in the left axilla, aspiration was not done because the area suggesting fluid was not large and the patient feared discomfort from the introduction of the needle. On May 3d the patient, having become more and more dyspneic and cyanotic, with irregular heart, died. The autopsy showed a greatly thickened pericardium, firmly adherent everywhere. There was no pericardial fluid. The left pleural cavity contained 500 c.c. of fluid. There were white dense areas over the liver and spleen—perihepatitis and perisplenitis—suggesting "Pick's disease." There was congestion of the lungs, a large liver, old thickening of the mitral leaflets, and small vegetations of the aortic leaflets.

In such a case what course of reasoning was to be pursued? At the time of entrance and during the entire course in the hospital she was never without a pericardial friction-rub. Usually when fluid begins to accumulate and thus to separate the serous surfaces of the sac, the friction-rub disappears. Fluid accumulates from the bottom up, so that the rub might disappear at the base. There was no retraction of the cardiac impulse, as in adherent pericardium. Broadbent's sign of adherent pericardium even if present in this case would have been obscured by the slowly accumulating hydrothorax. The dulness in the left back with bronchial breathing and egophony which she showed at entrance was thought then to be caused by an atelectasis due

to pericardial pressure—Ewart's sign—but later these signs changed to those of pleural effusion. If in adherent pericardium there do not happen to be adhesions between the pericardium and the diaphragm and lungs, then Broadbent's sign is absent. Christian, in a recent article, calls attention to a case in which there were very distinct signs of dulness beyond the area of cardiac impulse, which he says always suggest fluid, but sometimes a thickened pericardium will give the same thing. In our case the line of cardiac dulness was always well outside of the cardiac impulse. In chronically enlarged hearts, especially with a history of some old inflammatory process, it is not uncommon to have the cardiac impulse well within the left border of dulness. You can see that this patient offered considerable difficulty in diagnosis. The persistent to-and-fro friction-rub with such a large distribution was against the presence of fluid.

The *x*-ray plates were not different from a chronic myocarditis. One could feel sure only of a fibrinous pericarditis. There was no clinical evidence of an adherent pericarditis, and very little to suggest an effusion.

The second case is illustrative of pericardial effusion. A girl, fourteen years old, admitted to the hospital July 12, 1919, complaining of pain about the heart for eight days. The family history was unimportant. She had been well until a year before, when she had a long and severe attack of rheumatic fever, which left her with "heart trouble," although there were no symptoms, since she could run and play like other children. There had not been any other infections. No sore throat or tonsillitis. Her teeth were badly decayed.

The patient was perfectly well until eight days before admission, when her feet became red, swollen, and painful; later her hands were involved. There was no dyspnea, palpitation, nausea, or vomiting.

Physical examination showed a well-developed and nourished girl propped up in bed. There was dyspnea, an appearance of general discomfort, and an anxious expression. The chest showed poor expansion and shallow respiration. The left base behind was moderately dull, with bronchial breathing in an

area just below the angle of the scapula. Over both bases there were medium moist râles on inspiration.

The apex-beat, rather strong and diffuse, was best seen and felt in the fifth space in the left mammary line. Pulsations in the vessels of the neck were rather marked. The area of cardiac dulness extended from midaxilla on the left to 5 cm. to the right of the midsternal line. The cardiohepatic angle was obtuse. The sounds at the cardiac impulse were strong, regular, and rapid. Over the precordium, but loudest at the third space to the left of the sternum, was a to-and-fro friction-rub.

Having in mind the acute arthritis at onset of the present illness, the patient was started on salicylate of soda in full doses, and showed immediate improvement. The dyspnea became less, but no change took place in the friction-rub.

On July 19th the condition was not so good. The dyspnea was more marked, and the pericardial rub was heard over a more limited area along the right border and at the base. The signs about the angle of the scapula in the left base were more marked and were interpreted as Ewart's sign of compression.

The x-ray plates show a wide area at the fifth interspace—"water-bottle" shape. The cardiohepatic angle was, by percussion, unquestionably obtuse. The heart sounds were distant.

July 21st aspiration was performed in the fifth space just outside of the area of cardiac impulse and 350 c.c. of bloody fluid withdrawn. No organisms were obtained. The amount of fluid seemed smaller than the physical signs indicated, and, while the condition was improved, it was very transitory. Two days later a needle was inserted in the ninth space near the angle of the left scapula, with negative results, and in the fourth space to the right of the sternum, obtaining only a few cubic centimeters of dark blood. Following the second aspiration of the pericardial sac there was very slight improvement. The aspirations were done under local anesthesia, with a minimum of discomfort.

She gradually failed during the following week, the general condition not improving under any form of treatment, and died a week later. An autopsy was not obtained.

Here you see a child of fourteen years with a history of severe arthritis one year before, resulting in endocarditis, and a second attack eight days before entrance. The many carious teeth and pus cavities were sufficient foci. At entrance there were tender joints, dyspnea, orthopnea, and the anxious expression of labored breathing. There was a general improvement under treatment and hospital care which was only temporary. Gradually the to-and-fro friction-rub became less, the cardiac impulse less distinct, the sounds more distant, and the cardiohepatic angle more obtuse. With this was a development of pressure in the left back—Ewart's sign. Here was sufficient evidence of the formation of pericardial fluid, and aspiration proved the correctness of the signs. The fluid was bloody, which is unusual in rheumatic pericarditis, although I have seen it in a few cases. The sudden onset with infected joints did not leave much doubt as to the etiology of the pericarditis.

Let us briefly compare these cases. Both had foci of infection, acute arthritis, and cardiac disease before their last illnesses. The woman's last illness came on gradually, the child's, suddenly. Both had every evidence of fibrinous pericarditis upon admission to the hospital.

In the first case the rub was extensive and very loud almost the entire time in the hospital, and the heart area became a little smaller with rest in bed. In the child the rub became gradually less and the cardiac area larger; the cardiac impulse less distinct and the sounds more distant, as is the rule when the fluid accumulates anteriorly, and thus drives the heart further away from the chest wall. Both had enlarged hearts, one with effusion and one without, and yet you see that the plates are not dissimilar. Pain was marked in each case, a common symptom in rheumatic hearts, less easily noticed in pericarditis accompanying pneumonia, and often absent in the pericarditis of chronic nephritis and diabetes.

The woman's temperature soon dropped to 100° F. and became almost normal near the end, while her white count never exceeded 9400. The pulse seldom went above 100, and as the temperature came down it ranged between 80 and 90. The

child's temperature was between 102° and 104° F. until after the second aspiration, when it came down and ran a little above normal for a week before death. Her white count was 12,600. The pulse steadily rose until it reached 140. She gave every evidence of a more acute and active infection.

Sinnhuber believes that acute articular rheumatism is the most frequent cause of pericarditis, then pneumonia, tuberculosis, scarlet fever, influenza, typhoid, cerebrospinal meningitis, malaria, erysipelas, osteomyelitis, pyemia and sepsis, gonorrhea, scurvy, and leukemia. Certainly acute articular rheumatism causes more cases than any other infection, although from the above list it is clear that it should be carefully searched for during or after any acute infection. It may occur either by infection through the blood-stream or by extension from adjacent structures. Where there are attacks of tonsillitis, carious teeth, or evidences of focal infection the heart should be carefully and repeatedly examined, because even with very slight illnesses pericarditis may come on insidiously. It is our hope that the next generation of doctors will see much less cardiac disease, particularly in young persons, because focal infections are being sought for and removed before a serious general infection with heart involvement can occur. The 2 patients whose histories have been given might not have had their first attacks of arthritis with heart involvement had attention been given to their teeth and tonsils. Notwithstanding their damaged hearts after these first attacks, they might have gone on for years without additional cardiac disease had sufficient attention been paid to the eradication of foci. The first patient had small buried tonsils, often more dangerous than the greatly hypertrophied ones.

Considering the intimate relation of the pericardium with almost all of the structures of the thorax, it is not remarkable that pericarditis may be manifested in any portion of the thoracic viscera or even the abdominal, but more remarkable that it may exist without giving a sign. Cohnheim pointed out that complete obliteration of the sac was often enough a postmortem discovery for which no symptoms during life had prepared us. The symptoms of pericarditis are so varied and the onset so in-

sidious in some cases that Osler and almost every other writer has been led to say that many cases run their entire course without recognition. When it comes on very gradually and is the only manifestation of an obscure focus, or is well established when the patient comes under observation, it may not be detected. Examinations of the heart and lungs should be thorough, with subsequent daily examinations augmented by careful notes and cardiac measurements.

In our 2 cases pain was a prominent symptom, but this is not always so. It is by no means as constant as in pleuritis. The reason for this is not understood, perhaps because we do not know very much about the innervation of the heart. In the first case, which proved to be one of adherent pericarditis, you will notice that pain was constantly present and often quite severe, while in the second, pain disappeared as the fluid accumulated. Sears has called attention to the fact that pain may become quite severe when the fluid begins to form, but later the sac accommodates itself to the gradual distention, and the inflamed surfaces being no longer in apposition, the pain ceases or leaves in its place only a sensation of discomfort. McPhedran and Babcock speak of pain as a fairly constant symptom, while James Mackenzie, Poynton, and others emphasize the frequency of its absence. In 78 protocols which I studied it was mentioned in only 26 cases.

We have already spoken of the to-and-fro rub and the method of distinguishing it from murmurs. Sometimes a little extra pressure with the bell of the stethoscope helps to accentuate it. The grinding character of the rub is generally quite different from valve murmurs, and the latter have their characteristic signs in the circulation, although it must be remembered that murmurs often are present, but are obscured by the friction sound. The rub frequently moves from place to place over the precordia, while the position of murmurs is fairly constant. I cannot illustrate this point better than by recalling the following instance which I reported two years ago:

Three years ago, when looking for a case of aortic stenosis to show the students, I was told by the house physician of a

colleague, distinguished as a specialist in circulatory diseases, that they had a case. The patient, a man aged twenty-seven years, was convalescent from an acute multiple arthritis. He looked well and said that he was absolutely free of his discomforts. On listening to his heart he was found to have over the second interspace to the right of the sternum a rough, grating murmur, systolic in time. On listening carefully, however, a similar murmur, very faint, was heard in diastole. There were absolutely no cardiac or circulatory signs indicating aortic stenosis or regurgitation. In the absence of these confirmatory signs of valvular disease outside of the precordia, and taking into consideration the history of recent rheumatism, it seemed more probable that he had a precordial friction-rub. Two days later the rough sound, with its fainter diastolic, was heard over the third interspace to the left of the sternum, the following day over the fourth, and by the fifth day it was barely audible just above the cardiac impulse, and then disappeared.

The rub in both of our cases changed from time to time, and as it moved away from some of the valve areas endocardial murmurs were heard. In the text of the protocols we have discussed the significance of the disappearance of the friction sound and the signs of accumulating fluid. The two common causes of serous pericarditis are infection by some member of the rheumatic group and the pneumococcus. In the first the formation of fluid is often gradual and serous, as shown in our second case. During the pain and discomfort of acute pneumonia if fluid, usually purulent, forms it is apt to be overlooked if the patient succumbs to a rapidly spreading pneumonia with empyema. This was clearly shown by Major W. J. Stone in his series of cases at Fort Riley. On the other hand, if after the crisis the temperature begins to rise and to take on a septic variation, either empyema or pericarditis, or both should be suspected.

In the treatment of pericarditis, prophylaxis is of vast importance. Nothing could illustrate this better than the cases we have cited. In acute arthritis of the very mildest type absolute rest in bed is of vital importance. Bodily rest and

warmth as well as mental quiet will raise the general tone and resistance and thus materially assist in overcoming the infection, perhaps preventing cardiac involvement. Furthermore, it should be continued for at least two weeks after the infection has ceased. Inflamed tonsils should not be operated upon until every evidence of local and systemic infection has thoroughly subsided. I have known of 2 cases which ended fatally because of a too hasty operation. If there is increased rate of pulse with marked disturbance on slight exertion, accompanied by breathlessness, even without a to-and-fro rub, these are added reasons for absolute rest. As in acute pneumonia, the patient often assumes the position which he finds most comfortable. He should be propped up in bed on pillows, and, as McPhedran suggests, the use of the double inclined plane as used in surgical beds for the maintenance of the Fowler position will add materially to his comfort.

The patient should not be permitted to exert himself in any way, not even to alter his position in bed without assistance. There should be no straining at stool and the movements should be made soft and easy by a daily enema or the use of some simple cathartic. If when first seen there is a history of constipation, castor oil, if the dose is prepared so as not to cause vomiting, may be given, since it is important for the circulation and the subsequent management of the case to unload the intestine.

The diet should be light and easily assimilable. Soft-cooked eggs, soft toast, custards, well-cooked cereals, and a Salisbury meat cake occasionally will suffice. Milk with the addition of cream given slowly, cocoa or soups, will supply sufficient liquid. Food should be given in small amounts at frequent intervals. Small amounts of water may be given at a time, but it is well to keep the liquids low in quantity to prevent added strain on a laboring heart. Everything should be done to keep the digestion in as good condition as possible. In very mild cases the diet may be much more liberal, and in severe cases may be increased as convalescence progresses.

In practically every case at the Boston City Hospital we use the ice-bag over the precordia. It quiets the pain and

gives a sense of comfort. Even when there is no pain the patient prefers to continue its use. I always ask the patient if it gives him comfort, and he generally replies in the affirmative. Be sure that the ice-bag is not too heavy; it is sometimes an added burden to a laboring chest.

The application of blisters may be tried, especially in the beginning of fluid, sometimes with very satisfactory results. Blood-letting may be useful by applying ten or a dozen leeches over the precordia.

We have already spoken of the value of salicylate of soda in cases of pericarditis of arthritic origin. The earlier it is given, the better, and in as full doses as possible—20 grains every two hours. Its danger is that it is soon apt to upset the stomach, cause vomiting, and thus strain the embarrassed heart. The addition of 30 or 40 grains of bicarbonate of soda will sometimes prevent this result. It has been said that the salicylates are dangerous because they depress the heart, but it is more probable that the depression comes from toxemia. Codein or heroin in small doses may be used for cough and pain. Sleep is very important, as in all cardiac conditions, and is prevented by pain and restlessness. Generally cold and codein will give sufficient comfort to cause sleep. There is a universal distrust of chloral in this country, but since I heard five or six years ago that MacKenzie used it in cardiac dyspnea I have given it repeatedly in old degenerated, decompensated hearts with orthopnea and sleeplessness, with very satisfactory results. I generally give to an adult 10 grains and repeat the dose in one-half to three-quarters of an hour if necessary. Sometimes combined with  $\frac{1}{2}$  or  $\frac{1}{4}$  grain of morphin, where morphin has previously failed, its effects have been heightened, and I have never seen any untoward effects. I have not had occasion to give it in pericarditis, but I should not hesitate to give it if necessary.

In the discussion of the second case we spoke of the method used in aspirating. Many sites for paracentesis have been suggested, such as the left parasternal, the right parasternal, Marfan's epigastric xiphoid route, and the posterior route. As Curschmann says, no definite rule can be laid down in any case.

We must be guided by the area of dulness and the *x-ray*. I generally aspirate at one of two points according to the physical signs; either in the fifth space just outside the left border of cardiac dulness, or in the fourth space at the right margin of the sternum. If the needle is introduced slowly no harm will result if it touches the heart muscle. I have been able to find in the literature only 1 case where any harm resulted from wounding the heart. Byron Bramwell reports a case of continued hemorrhage into the pericardium from puncture of the ventricle. In rabbits, blood is removed from the ventricle without injuring the animal. In almost all articles authors speak of touching the heart with the needle.

In purulent pericarditis, exploratory aspiration determines the point of incision. In some cases where the fluid is posterior and the heart is pushed against the anterior chest wall it is necessary to aspirate in the back near the angle of the scapula.

Many cases with small amounts of serous effusion do not require aspiration, since the fluid is absorbed in a few days. In one of the large hospitals for children it has been stated that aspiration for serous effusion is rare.

Our case of adherent pericarditis was the same clinically as one of fibrinous pericarditis and hypertrophy. We did not recognize it as adherent pericarditis at the time, and our treatment would have been no different if we had. Adherent pericardium does not seem to do harm if the myocardium is not much involved, and there are no important adhesions between the surrounding viscera or the chest wall. These, of course, throw added work on the muscle and ultimately result in hypertrophy. Cardiolysis may be considered provided a polyserosis, such as existed in our case, can be excluded. After the removal of fluid various injections into the sac to prevent adhesions have been tried, but all have proved valueless.



## CLINIC OF DR. EDWIN A. LOCKE

BOSTON CITY HOSPITAL

### MALIGNANT DISEASE OF THE LUNGS PROBABLY SECONDARY TO A HYPERNEPHROMA OF THE KIDNEYS

THE history of the case which I shall discuss with you this morning is very meager, as so often happens in the case of hospital patients.

A carpenter of forty-five entered the hospital October 3, 1919 because of pain in the left chest.

**Family History.**—The patient's father died at forty-three, of pleurisy, and his mother at fifty-four, of pneumonia. One brother is living and well.

**Past History.**—When a small child the patient had scarlet fever, later measles, followed by pneumonia. He gives no history of any illness since childhood and has apparently been robust. He has never been subject to colds and can recall no attack of respiratory infection.

Venereal diseases are denied. Tobacco and alcoholic beverages in moderation. Best weight 170 pounds two years ago; 155 pounds a month ago.

**Present Illness.**—About five months ago he had a very severe headache which lasted without intermission for a month; since then occasional recurrence. Three weeks ago while working sudden onset of very sharp, knife-like pains in the left side of the thorax and lower back, which have persisted, though somewhat less severe. These pains are definitely exaggerated by deep respiration or cough. Associated with the pain has been an increasing distress in breathing, partly due, he thinks, to the pain, but more largely to a sensation of suffocation. A marked loss in strength has been noted and he also thinks he has lost weight. There has been no cough or sputum at any time and he has not been conscious of any fever.

DR. LOCKE: I will ask Mr. ——, to whom the case was assigned, to give us the results of his examination at the time of entrance.

CLINICAL CLERK: *Examination.*—The patient was well developed, but more or less emaciated, and gave the appearance of having been ill a long time. Marked weakness; skin and mucous membranes pale; respiration labored. The throat seemed normal, the lymph-nodes were nowhere found enlarged and the reflexes and sensations were normal.

The chest was symmetric, but the left showed much less expansion and lagged perceptibly. There were no dilated veins over the thorax. With the patient in a prone position the left front of the chest was slightly dull to percussion, which merged gradually into flatness in the axilla. Over the upper front on the left the respiration and fremitus were exaggerated in intensity, but not essentially changed in quality. A few scattered medium râles were heard. In the axillary region the respiration and fremitus were considerably diminished.

In the sitting posture the entire left back was dull, the note in the lower third being flat. The breathing was everywhere of the bronchial type, though much less intense over the upper half, and quite distant below the inferior angle of the scapula. The fremitus was increased above, of a quality suggesting egophony in the midscapular region, and slightly diminished below, yet of a distinct bronchial type. Tactile fremitus was present at the right base, but absent at the left. As in front, a few medium and coarse râles were heard over the back, more on the left than on the right. The right back seemed normal except for slight impairment of resonance below the angles of the scapula.

The heart was of normal size and normal position. The sounds were of rather poor quality and at the apex a soft blowing systolic murmur was heard.

Blood-pressure, 115/60. Temperature, 98.6° F. Pulse, 80. Respiration, 30.

Abdomen moderately distended, generally tympanitic; in the left hypochondrium and palpable 5 to 6 cm. below costal

border is a hard, very nodular, tender, and somewhat movable mass which descends slightly with inspiration. Its location seems deep in the abdominal cavity.

The urine showed the slightest possible trace of albumin and the sediment a few red blood-corpuscles, and an occasional hyaline and granular cast. No tubercle bacilli were found. The total two-hour phenolsulphonephthalein excretion was 40 per cent. and the blood urea nitrogen 25.6.

Blood examination: Hg. 50 per cent.; leukocytes 14,000; red count 2,400,000. Evidence in the stained smear of moderate secondary anemia. The differential count gave 74 per cent. polynuclear leukocytes.

DR. LOCKE: The obvious abnormalities in this case are the abdominal tumor and the condition in the left thorax. What is your interpretation of the signs in the chest?

CLINICAL CLERK: The signs are typical of consolidation, but I think there may have been fluid, or both.

DR. LOCKE: Bronchial respiration is, of course, typical of consolidation, but rarely this type of respiration may be heard over even a large pleuritic effusion. In many instances a diagnosis between the two can only be made by the needle. If a local anesthetic is used the procedure can be carried out with almost no inconvenience to the patient, and if the technic is faultless, without danger of complication. The combination of egophony in the midscapular region, flatness in the lower back, with distant breathing and absence of tactile fremitus strongly suggest fluid. Among all the signs of fluid the displacement of the heart and the absent tactile fremitus are, in my opinion, of the most significance. In this case the heart appeared to be in normal position.

An x-ray of the patient's chest was made soon after entrance, and apparently showed a moderate amount of effusion together with considerable mottling of the whole left lung as well as slight mottling of the right.

Thoracentesis was done on October 11th and 150 c.c. of very bloody serous fluid obtained. Cultures made from the exudate were sterile. The cells were mainly leukocytes, with a few of

the endothelial type. No tumor cells were found. What is the significance of a sanguineous fluid aspirated from the chest?

CLINICAL CLERK: It is, I think, always suggestive of malignant disease.

DR. LOCKE: Yes, and of tuberculosis, though it occurs with many other intrathoracic conditions.

A few blood-cells can be found microscopically in practically all pleural fluids, and microscopic blood may frequently be present after paracentesis of the chest due to injury to a blood-vessel or to puncture of the lung tissue. By hemothorax, however, we mean a pleural fluid which is definitely hemorrhagic. Any of the intrathoracic vessels may be the source of the blood, as a ruptured aneurysm, or from the erosion of a blood-vessel or rupture resulting from trauma. Occasionally a pleural transudate occurring in the course of chronic cardiac or renal diseases may be admixed with blood. Unless such a cause is evident, and this is very rare, a frank hemorrhagic pleural fluid points strongly to the presence of tuberculosis or malignant disease.

Before attempting to make a diagnosis between these two conditions I will give you further data on the case since his entrance to the hospital four weeks ago.

His general condition is less favorable than when first observed in the hospital. He is much weaker. Sputum was at first absent, but of late he has begun to raise, and now has several ounces daily of a thick, purulent, odorless character. Blood has never been noted in the sputum. There is no cough except to bring up the accumulated secretions. The difficulty in breathing has not perceptibly increased, but very slight exertion even in bed causes the respiration to be very labored and rapid. The temperature has remained normal at all times. Pain which was such a prominent feature in the early stages now gives him but little inconvenience. There have been no night-sweats. On October 4th the hemoglobin was 60 per cent., the white count 16,000 and the red count 2,600,000 per c.mm.; on October 15th hemoglobin 62 per cent.; white count 10,200, red count 2,700,000 per c.mm.

Many examinations of the sputum have failed to show the

presence of any tubercle bacilli and no type organisms have been found. On October 19th a second thoracentesis was done and 1000 c.c. of fluid withdrawn, which was more hemorrhagic than that obtained earlier. This fluid was sterile and no tumor cells were found. Immediately after this procedure a second x-ray examination of the chest was made, and the following report given by Dr. Ellsworth:

"Both lungs show increased density, with numerous more or less circular spots, varying in size from  $\frac{1}{2}$  to  $2\frac{1}{2}$  cm. in diameter, scattered throughout both lungs. These appear to have developed during the four weeks that the patient has been under examination. The appearances are typical of metastases from malignant growth not primary in the lungs."

Pus has never been present in the urine and only occasionally a few red blood-corpuscles.

Now with all the facts before you will you discuss the diagnosis as between a possible tuberculosis or malignant disease. What would you say regarding the patient's history?

**CLINICAL CLERK:** The history is probably very inaccurate and unimportant. It is evident that the course of the disease is much longer than given by the patient. It is not typical of tuberculosis. He has had no cough until very recently. It would be very unusual to have a tuberculous process of this advanced type without a very harassing cough. The symptoms of the present illness can be explained by either process.

**DR. LOCKE:** How much importance would you attach to his age?

**CLINICAL CLERK:** I should think his age was in favor of malignant disease.

**DR. LOCKE:** The fact that he is forty-five years old is slightly in favor of a neoplasm. The statement that his father died of pleurisy of course suggests that the disease might have been tuberculosis. Certainly there is no positive evidence of tuberculosis in his family or any known opportunity for contagion.

What other facts are important?

**CLINICAL CLERK:** The normal temperature is very much against tuberculosis, as it would be very unusual to have such

advanced tuberculosis of the lungs without fever. The leukocytosis if occurring with tuberculosis could be explained only on the basis of some secondary infection which does not seem to be present. On the other hand, an increased white count is almost always present in malignant disease.

Such a severe degree of anemia is characteristic of the latter disease and seldom seen with the former. With such an abundant sputum, if due to tuberculosis, the bacilli should be present.

DR. LOCKE: The *x*-rays furnish rather important data. You will see from an examination of the three plates made at intervals of seven to ten days that the infiltration of the lungs, and more especially the left, has developed rapidly. In the latest one the whole of both lungs is seen to be shadowed with irregular and quite distinct areas of variable size which are strongly suggestive of new growth. Such an appearance in the lungs might conceivably be found in disseminated tuberculosis, but it would be very atypical.

I agree that the evidence so far points strongly to malignant disease. The symptoms and signs of malignant disease of the lungs are extremely variable, and it is important to remember that in rare instances the process may progress to a surprising extent before there is evidence of its presence. This is sometimes the case when the signs and symptoms of the primary disease are so pronounced that the evidences of developing metastases in the lungs are entirely overlooked.

On the other hand, the symptoms may be very prominent and distressing. No symptoms or groups of symptoms can be set down as strictly pathognomonic of new growth of the lungs. The most constant and characteristic are dyspnea, cough, and character of the expectoration. Dyspnea when present is constant, progressive, and often extreme. Cough is apt to be a relatively early manifestation, but rarely appears only late in the course of the disease. It depends very largely as to its character and intensity on the secondary processes in the lungs accompanying or set up by the malignant growth. The sputum is not necessarily characteristic. In the early stages it is often absent. As in the case of the cough, its character depends on

the secondary processes set up in the lungs. Frequently the sputum has a prune-juice consistency and color, or is admixed with blood. Frank hemorrhage may occur. Rarely tumor masses can be found in the expectoration and a diagnosis made microscopically.

What form of new growth would you think most probable?

**CLINICAL CLERK:** Cancer is more common than sarcoma.

**DR. LOCKE:** Yes, and, what is of much greater importance, a primary growth of either type in the lungs or pleura is rare, sarcoma exceedingly so. It is so unusual that if no primary focus can be found you may be suspicious that your diagnosis of new growth of the lungs is incorrect. A sarcoma of the lungs is most commonly secondary to a sarcoma of bone-marrow (at least one-half the cases), but may also arise from a tumor of this type in the lymph-nodes or internal organs, as the kidneys. If the growth in the lungs is carcinoma, it is most frequently due to metastases from a cancer of the breast. Cancer of the abdominal viscera and the prostate also often metastasize in the lungs. Apropos of this fact the signs in the abdomen in this case are of the greatest moment.

Now let us consider the mass which you describe in the abdomen. First, what structure do you think is involved? What is the exact location of the mass?

**CLINICAL CLERK:** It seems to be deep in the lumbar region protruding from under the right border. It is readily felt bimanually and descends slightly with deep inspiration. With the position so definite it cannot be in the left lobe of the liver or the stomach. It may be the spleen, but there is no notch to be felt, and the position is more deep and more toward the median line than would be the case were it an enlarged spleen. Although somewhat high in position, a tumor of the splenic flexure of the colon is a possibility, but the position is so characteristic of kidney that I think the tumor felt is probably an enlarged kidney.

**DR. LOCKE:** A very thorough x-ray examination of the gastro-intestinal tract has been made by Dr. Butler, and no evidence of disease of the stomach or intestines was found. An

especially important result of this examination is that the colon was shown to be in front of the tumor. This *x*-ray report is sufficient to rule out the colon as the seat of the disease. The *x*-ray examination of tumors of the kidney is almost always very unsatisfactory. The position of the tumor which you have described leaves little room for doubt that it is the kidney which is felt.

What is the evidence that the mass is malignant?

**CLINICAL CLERK:** The characteristics mentioned are very typical of a neoplasm. Such a hard nodular mass could hardly be anything else.

**DR. LOCKE:** We have surprisingly little in the history of the case to fortify us in the diagnosis of a malignant tumor of the kidney. Of the three cardinal symptoms of the condition—namely, pain, hematuria, and tumor—we have a record of only the last. The mass is quite sensitive to pressure and we now have the story from the patient that he has had a great deal of dull and nearly constant pain of late in the left lumbar region. The pain in tumor of the kidney is extremely variable. It may appear early or be absent until a late stage of the disease. He has never noted any hematuria and none has been present since he came to the hospital. Only a few red blood-corpuscles have occasionally been found microscopically. Profuse and recurrent hemorrhage from the kidney is a very common symptom when the organ is the seat of malignant disease. Frequently the hemorrhage continues for several days and is very profuse. Clots and even casts of the ureters may be present in the urine.

In hypernephroma, however, it is not uncommon to find the urine practically normal until a late stage of the disease. Even in advanced disease of this type the kidneys may remain functionally good, as indicated by the renal function tests. The figures given for the phthalein excretion and the blood urea nitrogen in this case are only moderately abnormal.

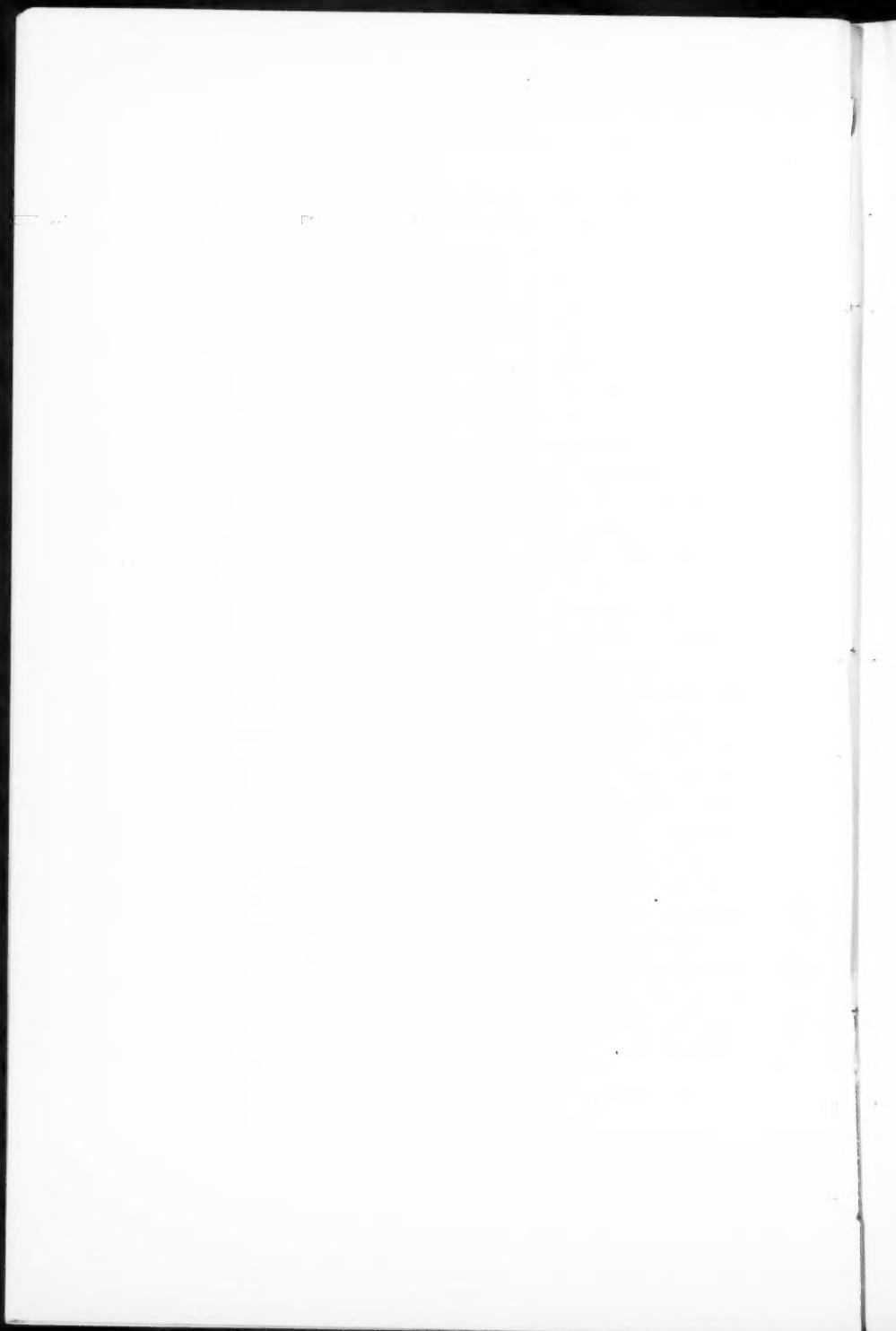
**CLINICAL CLERK:** Can you positively exclude tuberculosis of the kidney in this case?

**DR. LOCKE:** Your question is a very reasonable one. In the first place this case illustrates a very important principle in

diagnosis which I want especially to emphasize. It is that when a definite pathologic condition is present you should, if possible, connect symptoms in other parts of the body with it, in other words, explain as much as possible by a single disease. The chances are always much in favor of one disease being responsible directly or indirectly for all symptoms rather than multiple diseases. In this instance everything seems to indicate that the condition in the lungs is due to malignant disease and of secondary type. If so, there must be a primary focus, and one of the commonest points of origin is the kidney. Hence the inference is fully warranted that a tumor mass of the type found here is the origin of the process in the lungs and not an entirely distinct and separate disease. Were the trouble in the lungs due to tuberculosis, then, as truly, any evidence of disease in the kidney would, in all probability, be of the same nature. Under these circumstances we must have proof that the disease in question is present and not that it is absent.

Now as to your question: The hard, nodular tumor felt in the abdomen is not like a tuberculous kidney. There is no fever. We have no evidence of this disease elsewhere in the body. To be sure, renal symptoms of such a disease in the kidney may be wanting until a relatively late stage, but here, where we have no other evidence of tuberculosis of this organ, their absence is especially significant. There is no polyurea, especially at night, no burning with micturition, no hematuria, and no pus or tubercle bacilli in the urine. I can see no evidence of tuberculosis of the kidney.

Besides illustrating admirably the symptoms and course of secondary new growth of the lungs, this case shows the necessity for careful and exhaustive study of an obscure type of case like this one, and finally, the principle of correlation of disease conditions in various parts of the body.



CONTRIBUTION BY DR. M. J. ROSENAU

HARVARD MEDICAL SCHOOL

**STUDIES IN FOOD POISONING—AN EXPERIMENTAL  
LUNCH WITH CANNED FOOD CONTAINING BAC-  
TERIA**

A GROUP of workers in the Department of Preventive Medicine and Hygiene, at Harvard, has devoted their entire time during the last two years to a study of food poisoning with special reference to canned goods. In studying the bacteriology of this problem we asked ourselves the question: "Are the contents of merchantable canned goods always sterile?" In order to answer this question we studied a large number of canned products bought in the open market. These samples represented a great variety of foods—meats, fish, shell-fish, fruits and vegetables, milk, and soups. Care was taken to purchase standard brands of first quality, packed in all different parts of the country, so as to have a representative average.

We assumed from the standpoint of our general bacteriologic knowledge that probably some of the hardy, resisting spores would survive the time and temperature used in processing. This turned out to be the case. In other words, living bacteria may be present in cans, although the food gives no evidence of spoilage. Professor John Weinzirl, Dr. E. W. Cheyney, and Miss Madeline Tschaler examined 1750 cans of prime, merchantable foods, and found about 12 per cent. of them to contain viable micro-organisms. These were, for the most part, the spores of the ordinary aërobic bacteria, such as *Bacillus subtilis* and *B. mesentericus*. No evidence of multiplication of these micro-organisms was disclosed by the methods used, and

the contents of the cans in question were normal<sup>1</sup> in taste, odor, and appearance.

Professor Weinzirl studied 782 "commercial" or market samples, of which 104 were fruits, 370 vegetables, 273 meats, and 35 milks. By "commercial" or merchantable is meant canned goods obtained through the ordinary sources of trade. For the most part, the cans were bought on the open market, with the exception of some marketable samples received from more than 50 canners distributed over the entire United States, in order to insure geographic representation of the samples examined. Weinzirl concluded that:<sup>2</sup>

1. Commercial canned foods, as found in the markets, are not always sterile, but may contain viable spores of bacteria.
2. The living spores found in commercial canned foods are unable to grow in the food, due to the absence of oxygen.
3. The vacuum is essential to the preservation of canned foods under present methods of processing.
4. Food poisoning organisms, such as *Bacillus botulinus*, *B. enteritidis*, etc., are not found in commercial canned foods.<sup>3</sup>

Ever since the days of Appert (1804), the Parisian confectioner who first demonstrated the practicability of preserving food by heating and hermetically sealing to exclude air, great importance has been placed upon the latter point by practical men in the

<sup>1</sup> By "normal" in this connection is understood a taste, flavor, and appearance which would have permitted the use of the cans in question by a careful housekeeper. The term "normal" does not apply to products which have undergone such a slight change that can be detected only by an expert in these matters.

<sup>2</sup> The Bacteriology of Canned Foods, Jour. Med. Research, January, 1919, xxxix, 3, pp. 349-413.

<sup>3</sup> This means that neither *Bacillus botulinus* nor *B. enteritidis* were found in any of the cans examined. Weinzirl's conclusion No. 4 is perhaps too inclusive, although the inference seemed warranted from the facts then at hand. The heat of processing canned goods will surely kill non-spore-bearing organisms of the typhoid-colon group. With a few rare exceptions botulism has not been traced to "commercial" canned goods, and almost all the cases have been caused by food processed in the home. In Germany most of the cases are referable to sausages and hams. A thorough investigation of the whole question of botulism is being made in the laboratory of the Department of Preventive Medicine and Hygiene, at Harvard, and a monograph of the subject is in preparation.

canning industry. When bacteriologists showed that spoilage was due to the growth and development of micro-organisms, the importance of the vacuum was belittled, for all bacteriologists know that sterile media in a tight container will keep indefinitely, whether oxygen is present or absent. This was one of Pasteur's classic experiments. Now that we realize that canned goods are not always sterile, the practical importance of the vacuum again deserves consideration.

On account of the importance of this subject the studies started by Dr. Weinzirl were continued by Dr. Cheyney, who examined 725 cans, advancing the subject and throwing further light upon it. Dr. Cheyney's results will be found in his paper presented in the Journal of Medical Research, July, 1919, pp. 177-197. Dr. Cheyney states that "seven hundred and twenty-five cans of merchantable foods in prime condition were carefully examined for bacteria, molds, and yeasts. The range of materials was wide, including the usual market brands of meat, fish, vegetables, and fruits. All samples examined were purchased in the open market. Before analysis each can was incubated at 37° C. for at least ten days. Special precautions were taken to exclude outside contamination during examination, and particular media were used to assure the growth of any organism that might be present in the sample. Fifty-eight out of seven hundred and twenty-five, or eight per cent. of these cans, were found to contain living micro-organisms. Not all foods contained organisms, some being found always sterile, some with a constantly low percentage, others with a high percentage of cans containing viable organisms. There was a uniform average found throughout for each food; vegetables being sterile or showing only a small number of cans containing viable organisms (8 per cent.), fruits showing a consistently lower number (3 per cent.), fish and meats varying from 10 to 20 per cent. The organisms isolated constitute a sharply limited group of resistant spore-bearers, including the *Bacillus subtilis mesentericus* group, the related thermophiles, an anaerobe, four common species each of *Aspergillus* and *Penicillium*, and two border-line yeasts. No pathogenic organisms were found. The bacteria were associated chiefly with the meats, while the

molds formed the sole flora of all the fruit cans found to contain living organisms. Thermophiles were found only in crab and lobster. There was evidence to suggest that in certain foods the bacteria and molds had persisted through the processing, and that the usual methods of processing must be increased to obtain actual sterility in these foods."

The next question that logically arose from this situation was: "Does food containing these viable organisms have any ill effect upon health?" The only answer to this question could be had by eating the food in question and watching the results. We therefore organized an experimental lunch club, made up of the laboratory staff, at which the contents of the cans examined by Professor Weinzirl, Dr. Cheyney, and Miss Tschaler were eaten.

#### THE EXPERIMENTAL LUNCH

**Time.**—The experimental lunch was started March 4, 1918, and continued until July 1, 1919—a period of sixteen months—thereby giving opportunity to observe the effects of the food on trial during all seasons, including two summers, and under a great variety of conditions.

The experimental food was eaten four days a week, namely, Monday, Tuesday, Wednesday, and Thursday (Friday only during the summer months), making a total of over 256 meals.

**Personnel.**—There were usually between fifteen and twenty at the lunch table—never less than ten, and often twenty-four, which was the full membership of the crew. All the persons who volunteered for this experiment were members of the Department of Preventive Medicine and Hygiene and the Department of Pharmacology at the Harvard Medical School. The personnel had an intelligent interest in the experiment, and we had the further advantage of keeping in close touch with and constant supervision of the health of each individual.

**Controls.**—Each meal was arranged so that the luncheon of a certain number of the volunteers consisted of the experimental food, while the remaining members at the table were given other fare. In this way we always had controls not only of the experimental food but also of the other food served and eaten.

A large specimen (approximately one-third) of the contents

of each can of experimental food was kept in reserve in the ice-box under bacteriological precautions for further study in case of sickness.

**Records.**—A complete record of each detail of the experiment was kept from day to day. Each individual signed a slip showing just what he had eaten. Thus:

July 4, 1918.	Prof. Ro.
Corn, can no. 1492.	
Bread and butter	
Lettuce salad	
Coffee	
Strawberry jam.	
(Signed) M. J. R.	

In addition, an account was compiled of each day's operations, an example of which is given in the illustrative record which follows:

Name	Experimental Lunch-Tuesday, April 29, 1918.						Remarks
	Poisonous Corn #501	Poisonous Corn #502	Poisonous Corn #444	Poisonous Corn #465	Poisonous Corn #509	Poisonous Corn #514	
P.	+	+	+	+	+	+	
B.	+	+	+	+	+	+	
A.	+	+	+	+	+	+	
D.	+	+	+	+	+	+	
C.	+	+	+	+	+	+	
E.	+	+	+	+	+	+	
G.	+	+	+	+	+	+	
H.	+	+	+	+	+	+	
I.	+	+	+	+	+	+	
J.	+	+	+	+	+	+	
K.	+	+	+	+	+	+	
L.	+	+	+	+	+	+	
M.	+	+	+	+	+	+	
N.	+	+	+	+	+	+	
O.	+	+	+	+	+	+	
P.	+	+	+	+	+	+	
Q.	+	+	+	+	+	+	
R.	+	+	+	+	+	+	
S.	+	+	+	+	+	+	
T.	+	+	+	+	+	+	
U.	+	+	+	+	+	+	
V.	+	+	+	+	+	+	
W.	+	+	+	+	+	+	
X.	+	+	+	+	+	+	
Y.	+	+	+	+	+	+	
Z.	+	+	+	+	+	+	

Can No.	Food.	Brand.	Condition of can.	Taste, odor, appearance.	Time and temperature of incubation of cans prior to eating contents.	Result of bacteriologic examination.
464	Pumpkin	C.	Normal—no gas	Good	13 days at 37° C., then 12 days at 20° C.	B. Mesentericus
465	Pumpkin	H.	Normal—no gas	Good	13 days at 37° C., then 12 days at 20° C.	B. Subtilis
537	Pumpkin	W.	Normal—no gas	Good	24 days at 37° C.	B. Mesentericus
538	Pumpkin	W.	Normal—no gas	Good	24 days at 37° C.	None
539	Raspberries	S.	Normal—no gas	Good	14 days at 37° C.	B. Mesentericus
540	Raspberries	S.	Normal—no gas	Good	10 days at 37° C.	Aspergillus Nidulans
541	Raspberries	S.	Normal—no gas	Good	10 days at 37° C.	None
54	Pears	E.	Normal—no gas	Good	20 days at 37° C.	B. Thermoindifferens

**Experimental Food.**—The experimental food consisted of canned goods that had been incubated at 37° C. for a variable time, rarely less than ten days, usually two to four weeks, and often longer. In addition to this, the cans were exposed to the ordinary temperatures of storage and transportation, both in the trade and in the laboratory. Opportunity was thereby afforded for the growth and development of bacteria at a wide range of temperatures.

The canned goods in question were all good quality of merchantable goods bought in the open market. The cans were always opened in the morning before lunch, examined bacteriologically, and then scored for odor, appearance, and taste.

**Preparation.**—The experimental food was eaten without cooking. Some of the samples were prepared as salads in order to render them more palatable.

**Number of Cans.**—Seventeen hundred and fifty cans of experimental food were eaten at the lunch table, each of which was carefully examined bacteriologically. In addition, many other canned and fresh foods were eaten, of which samples and records were kept, but they were not analyzed.

#### BACTERIOLOGIC STUDY OF THE CANNED GOODS EATEN

The results of the bacteriologic studies of the canned food eaten at the experimental lunch are summarized in the following:

Seven hundred and eighty-two cans were examined by Weinzirl, who found 179, or 23 per cent., to contain living microorganisms, mostly spore-bearing bacteria. The results appear in the table shown on page 920.

*Showing percentage of sterile and contaminated samples of the  
canned foods examined.*

Serial Number.	Food.	Number of Cans Examined.	Number Sterile.	Number Not Sterile.	Per Cent Not Sterile.
1.	Apples	7	5	2	28.5
2.	Apricots	11	11	0	0.0
3.	Blueberries	11	8	3	27.2
4.	Peaches	13	7	6	46.1
5.	Pears	18	13	5	27.7
6.	Plums	11	2	9	81.8
7.	Pineapple	13	11	2	15.4
8.	Raspberries	20	12	8	40.0
9.	Asparagus	18	15	3	16.6
10.	Beets	6	6	0	0.0
11.	String Beans	40	32	8	20.0
12.	Lima Beans	11	9	2	18.2
13.	Kidney Beans	0	7	2	22.2
14.	Baked Beans	14	10	4	28.5
15.	Corn	53	44	14	24.1
16.	Hominy	16	14	2	14.2
17.	Okra	7	2	5	71.4
18.	Peas	53	45	8	15.1
19.	Sweet Potatoes	6	6	0	0.0
20.	Pumpkin	26	18	8	30.8
21.	Sauerkraut	12	12	0	0.0
22.	Spaghetti	44	31	13	29.5
23.	Spinach	6	6	0	0.0
24.	Tomato	43	31	12	27.9
25.	Corned Beef	16	8	8	50.0
26.	Oysters	9	9	0	0.0
27.	Shrimp	36	26	10	27.7
28.	Salmon	17	15	2	11.8
29.	Sardines	181	140	41	22.6
30.	Tongue	8	6	2	25.0
31.	Evaporated Milk	23	23	0	0.0
32.	Condensed Milk	12	2	10	83.3

The bacteria found in the above are listed in the following table:

*List of bacteria found in canned foods.*

No.	Name.	Times Found.	Description by
1.	<i>B. mesentericus</i> (Flügge)	117	Ford et al.
2.	<i>B. subtilis</i> (Cohn)	51	" " "
3.	<i>B. vulgatus</i> (Flügge)	27	" " "
4.	<i>B. cereus</i> (Frankland)	21	" " "
5.	<i>B. welchii</i> (Migula)	6	Chester.
6.	<i>B. thermoindifferens</i> (N. S.)	35	N. S.
7.	<i>B. aërothermophilus</i> (N. S.)	6	N. S.
8.	<i>B. thermoalimentophilus</i> (N. S.)	2	N. S.
9.	<i>B. stearophilus</i> (N. S.)	4	N. S.
10.	<i>B. circulans</i> (Jordan)	7	Ford et al.
11.	<i>B. vulgaris</i> (Houser)	5	Chester.
12.	<i>B. cloacæ</i> (Jordan)	4	Chester.
13.	<i>Bact. aërogenes</i> (Escherich)	3	Chester.
14.	<i>B. coli communis</i>	11	Chester.
15.	<i>B. coli communior</i>	4	—
16.	<i>B. pseudoletanicus</i> (Kruse)	4	Ford et al.
17.	<i>B. lactis vinus</i> (Conn)	4	Conn et al.
18.	1 f. ( <i>Ps. pseudotuberculosis</i> [?], Conn)	6	—
19.	<i>B. laterosporus</i> (Laubach)	2	Ford et al.
20.	<i>B. agri</i> (Laubach and Rice)	2	" " "
21.	15a ( <i>Ps. lactis anana</i> [?], Conn)	2	Conn.
22.	S 69a ( <i>B. cuticularis</i> , Tils)	2	Chester.
23.	Str. lacticus (Kruse)	19	Conn et al.
24.	Sar. lactis albus (Conn)	16	" " "
25.	Sar. lactis acidi (Conn)	8	" " "
26.	Sar. alba (Zimmerman)	9	Chester.
27.	M. lactis albidus (Conn)	2	Conn.
28.	Strpx. foersteri (Cohn)	3	Chester.
29.	All other bacteria	12	Chester.

Dr. Cheyney examined 725 cans, the results of which are shown in the following table:

*Foods examined, showing the number and percentage of cans of each food found to contain viable organisms.*

Kinds of Food.	Number of Cans Examined	Cans Containing Viable Organisms.	
		No.	Per cent.
<i>Meats:</i>			
Sausage . . . . .	39	7	18
Corned beef . . . . .	40	7	18
Chicken . . . . .	45	4	9
<i>Fish:</i>			
Salmon . . . . .	34	7	20
Sardines . . . . .	33	3	9
Lobster . . . . .	25	1	4
Shrimp . . . . .	53	4	8
Crab . . . . .	23	6	25
Tuna fish . . . . .	26	2	8
<i>Vegetables:</i>			
Beets . . . . .	28	4	14
Asparagus . . . . .	26	2	8
Beans . . . . .	38	3	8
Peas . . . . .	33	0	0
Pineapple . . . . .	62	0	0
<i>Fruits:</i>			
Raspberries . . . . .	33	1	3
Pears . . . . .	43	1	2
Plums . . . . .	47	2	4
Peaches . . . . .	46	3	7
Apricots . . . . .	51	1	2
	725	58	8%

The organisms found in the above cans and the particular food with which they were associated are listed in the table on page 923.

## Organisms found, and the foods from which they were isolated

Organism.	Foods.
<i>Bac. vulgatus</i> (Flügge) . . . . . 10 specimens	Salmon (3), corned beef (3), beans, beets, peas, chicken.
<i>cereus</i> (Frankland) . . . . . 6 specimens	Crab (2), sausage (2), beets, shrimp.
<i>mesentericus</i> (Flügge-Migula) . . 5 specimens	Crab, chicken, sausage, corned beef, peas.
<i>simplex</i> (Ford <i>et al</i> ) . . . . . 4 specimens	Sausage, sardines, asparagus, tuna fish.
<i>megatherium</i> (DeBary) . . . . . 3 specimens	Chicken (2), salmon.
<i>cohaerens</i> (Gottheil) . . . . . 2 specimens	Beets, shrimp.
<i>subtilis</i> (Cohn) . . . . . 2 specimens	Shrimp, peas.
<i>thermophilus</i> IV (Rab) . . . . . 2 specimens	Crab, lobster.
<i>petasites</i> (Gottheil) . . . . .	Shrimp.
<i>pseudo-tetanicus</i> (Ford <i>et al</i> ) . . . . .	Corned beef.
<i>anaerobus</i> VIII (Sanfelice) . . . . .	Crab (Walfischrausch brand [Obst]? Symptomatic anthrax [Chester]?)
<i>Staphylococcus albus</i> . . . . .	Sausage.
<i>aureus</i> . . . . .	Sardines.
<i>Penicillium decumbens</i> (Thom) . . . . .	Chicken.
<i>expansum</i> (Thom) . . . . .	Raspberries.
<i>intricatum</i> (Thom) . . . . .	Crab.
<i>niger</i> (Thom) . . . . . 3 specimens	Peaches (3).
<i>Aspergillus fumigatus</i> (Thom) . . . 2 specimens	Raspberries (2).
<i>nidulans</i> (Thom) . . . . . 2 specimens	Peaches, apricots.
<i>glaucus</i> (Thom) . . . . .	Sardines.
<i>ochraceus</i> (Thom) . . . . .	Raspberries.
<i>Mycoderma hyalospora</i> (?) (Hansen), 2 specimens	Crab (2).
<i>Saccharomyces anomalus</i> (Hansen) . . . . .	Peaches,
sp (Hansen) . . . . .	Beets.
<i>Oidium</i> , sp . . . . .	Beets,
<i>Cladophorix dichotoma</i> . . . . .	Plums.

In addition to the above, a series of 261 cans was examined by Miss Tschaler, with the following results:

FOODS EXAMINED, SHOWING THE NUMBER AND PERCENTAGE OF CANS OF EACH FOOD FOUND TO CONTAIN VIABLE ORGANISMS

Kinds of food.	Number of cans examined.	Cans containing viable organisms.	
		No.	Per cent.
<b>Meats:</b>			
Sausage.....	15	0	0
Corned beef.....	29	0	0
Chicken.....	6	0	0
<b>Fish:</b>			
Salmon.....	18	0	0
Shrimp.....	26	1	4
Crab.....	20	2	10
<b>Vegetables:</b>			
Beets.....	18	1	6
Kidney beans.....	5	0	0
Peas.....	25	2	8
Pineapple.....	23	0	0
<b>Fruit:</b>			
Raspberries.....	18	2	11
Pears.....	14	0	0
Peaches.....	21	3	14
Plums.....	10	0	0
Apricots.....	13	0	0
<b>Total.....</b>	<b>261</b>	<b>11</b>	<b>4.5</b>

The organisms found in the above cans and the particular food with which they were associated are listed in the table on page 925.

ORGANISMS FOUND, AND THE FOODS FROM WHICH THEY  
WERE ISOLATED

Organism.	Foods.
<i>B. subtilis</i>	2 specimens
<i>B. mesentericus</i>	1 specimen
<i>Asp. ochraceus</i>	1 "
<i>Asp. niger</i>	3 specimens
<i>Asp. fumigatus</i>	1 specimen
<i>Pen. expansum</i>	1 "
<i>Thermophiles</i>	1 "
<i>Anaerobes</i>	1 "
Yeast	1 "

## RECORD OF ILLNESS

We were in a fortunate situation so far as keeping in close touch with the health of each member of the lunch club was concerned. Furthermore, we had the advantage of intelligent co-operation.

There were the expected incidence of headaches, common colds, indigestion, and occasional diarrheas among those who ate the experimental food. None of these, however, was believed to be due to the food in question. It is significant to note the frequency with which gastro-intestinal upsets occurred on Sunday and Monday. A brief summary of every case of illness that in any way might be referable to the experiment follows:

## CASE No. 1.—Dr. Mor. (Japanese), age thirty, March 4, 1918.

At 5.30 p. m. had a slight abdominal pain. At 8 p. m. took supper, which consisted of chicken soup, fish cake, string beans, mince pie, and fruit (orange and peach). At midnight had a slight feeling of chilliness and had three watery stools between then and 7 A. M., when all symptoms ceased. No headache. Temperature 97° F., pulse 72.

History of food eaten for five days prior to attack is as follows:

February 27th—Breakfast: Bread, butter, honey, milk, eggs, tea.  
Luncheon: American chop suey, bread, butter, tea, apple pie.  
Supper: Rice, mixed vegetables, chicken and vegetables, tea.

February 28th—Breakfast: Bread, butter, honey, milk, eggs.  
Luncheon: Two sandwiches of eggs and ham, coffee.  
Supper: Steak, vegetable soup, rice, tea. Apple, cake, glass of ginger ale.

March 1st—Breakfast: Bread, butter, honey, milk, eggs.  
Luncheon:  
Supper: Steak, vegetable, eggs, soup, rice, apple, tea.

March 2d—Breakfast: Bread, butter, honey, milk, eggs.  
Luncheon: Two ham sandwiches, coffee.  
Supper: Vegetable soup, chicken chop suey, rice.

March 3d—Breakfast: Bread, butter, orange marmalade, milk, eggs.  
Luncheon: Milk and crackers.  
Supper: Rice, chicken and vegetables, fish, tea, cocoa, candy.

March 4th—Experimental: Corn, can No. 300.  
Incubated eleven days at 37° C.  
Bacteriologic examination—sterile.  
Score—Normal in taste, odor, and appearance.  
Control—Miss Hus. ate contents of same can without ill effects.

*Remarks.*—This case followed our first experimental lunch, and was the subject of much friendly bantering and teasing, which Dr. Mor. took seriously. He became nervous and very much frightened about the possible outcome. He probably had a "nervous diarrhea" which is not uncommon, aggravated by chilling in a snowstorm, which he stated was apt to give him a diarrhea.

CASE No. 2.—Miss C., age twenty-two, Saturday, March 16, 1918.

"On the morning of March 16th I had a severe abdominal pain which lasted for two to three hours. I tried to get up and fainted, feeling faint up to Saturday noon. On the Friday previous, March 15th, I felt nauseated during the day, and had a slight headache." Rapid recovery.

*Experimental Food.*

March 12th—Beans, can No. 321.

Incubated twelve days at 37° C.

Bacteriologic examination—sterile.

Score—Normal odor, taste, and appearance.

Controls—Mr. Ba. ate contents of same can, with no ill effects.

March 13th—No experimental food.

March 14th—Sweet potatoes, can No. 334.

Incubated seventeen days at 37° C.

Bacteriologic examination—sterile.

Score—Normal odor, taste, and appearance.

Controls—Mr. Ba., Mr. A., Prof. Br., Dr. Bi., Miss D., and Miss Hus. ate contents of same can without ill effects.

March 15th—No experimental lunch (Friday).

*Remarks.*—Symptoms came on about forty hours after eating experimental food, which was sterile, and which was eaten by 6 other persons, none of whom became ill.

CASE No. 3.—Mr. Ba., age twenty-eight, Monday, April 1, 1919.

"I had cramps in stomach at 6 P. M. Pains in left side at 8 A. M., April 2d. Pains in left side at 11 A. M. No other symptoms."

*Experimental Food.*

March 30th—No experimental food.

March 31st—No experimental food.

April 1st—Spinach, can No. 412.

Incubated seventeen days at 37° C.

Bacteriologic examination—sterile.

Score—Normal odor, taste, and appearance.

Controls—Miss Fa., Dr. I., Dr. We. ate contents of same can without ill effects.

*Remarks.*—Symptoms started five hours after eating experimental food, which was sterile and was eaten by three other persons without ill effects.

CASE No. 4.—Mr. S., age twenty-eight. Monday, April 1, 1918.

"Headache all the afternoon, commencing at about 2 o'clock

and gone about 8 P. M. (after eating). Probably not due to excessive smoking. No other symptoms."

*Experimental Food.*

March 30th—No experimental food.

March 31st—No experimental food.

April 1st—Spinach, can No. 411.

Incubated seventeen days at 37° C.

Bacteriologic examination—sterile.

Score—Normal odor, taste, and appearance.

Controls—Miss Ma., Prof. Hu., and Miss Gr. ate contents of same can without ill effects.

*Remarks.*—Symptoms came on less than two hours after eating experimental food, which was sterile, and was eaten by three other members of the lunch club without ill effects.

CASE No. 5.—Mr. Go., aged twenty-two. Tuesday, April 2, 1918.

Slight pain felt in epigastric region at 10 A. M. on April 2d, lasting about two hours.

*Experimental Food.*

March 30th—No experimental food.

March 31st—No experimental food.

April 1st—Spinach, can No. 410.

Incubated seventeen days at 37° C.

Bacteriologic examination—sterile.

Score—Normal taste, odor, and appearance.

Controls—Miss Hus., Miss K., and Prof. W. ate contents of same can without ill effects.

*Remarks.*—Symptoms came on twenty-two hours after eating experimental food, which was sterile, and was eaten by three other persons without ill effects.

CASE No. 6.—Prof. Br., age thirty-five. April 4, 1918.

"About 4.30 in the afternoon of April 4th I began to feel a slight dull, but continuous pain, in the abdomen. The feeling resembled that of precursor of a diarrhea. At lunch had beans." No other symptoms.

*Experimental Food.*

April 2d—String beans, can No. 416.

Incubated fourteen days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in taste, odor, and appearance.

Controls—Mr. Go. and Dr. We. ate contents of same can without ill effects.

April 3d—No experimental lunch (corn chowder).

April 4th—No experimental lunch (cooked beans).

**Remarks.**—Experimental food was eaten two days before symptoms came on. The contents of the same can were eaten by two other people without ill effects.

**CASE No. 7.**—Prof. Hu., age forty-five. Sunday, April 7, 1918.

Appetite poor all day. About 5 p. m. ate two pieces of candy. Within about an hour began to feel nausea. Then had a loose movement. Another during the evening. Monday, April 8th, feeling seedy. Two loose movements in morning. Slight cramps. Prompt recovery.

*Experimental Food.*

April 4th—Red kidney beans, can No. 435.

Incubated fourteen days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—Professor Br. and Dr. I. ate contents of same can with no ill effects.

April 5th—No experimental luncheon.

April 6th—Squash, can No. 150.

Incubated four days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—None.

Also—Peaches, can No. 444.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—Contents of same can eaten by Miss Gr., Dr. I., Dr. Mor., Mr. S., and Professor W. with no ill effects.

**Remarks.**—Attack came on Sunday at 5 p. m., about twenty-nine hours after eating experimental food (squash and peaches), which were sterile and eaten by 5 others without ill effects.

CASE No. 8.—Mr. Ba., age thirty. Wednesday, April 17, 1918.

Symptoms started at 7 P. M. with nausea and cramps, some fever, no diarrhea. Lasted until midnight. Next day (April 18th) there was a recurrence of the nausea and cramps, some fever, no diarrhea. Prompt recovery.

*Experimental Food.*

April 15th—Corn, can No. 495.

Incubated twenty-three days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in taste, odor, and appearance.

Controls—Mr. Go., Miss K., and Professor W. ate contents of same can with no ill effects.

April 16th—Oysters, can No. 506.

Incubated six days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in taste, odor, and appearance.

Controls—Contents of can eaten by Dr. Bi. and Mr. S. with no ill effects.

April 17th—Okra, can No. 518.

Incubated twenty-five days at 37° C.

Bacteriologic examination—*Bacillus mesentericus*.

Score—Normal in taste, odor, and appearance.

Controls—Miss Hus. ate contents of same can with no ill effects.

*Remarks.*—The okra eaten at noon was contaminated with spores of *Bacillus mesentericus*. The symptoms came on about seven hours later. This is the only instance in which symptoms followed the eating of canned goods containing bacteria. Another member of the lunch club ate contents of the same can without ill effects.

CASE No. 9.—Prof. Hu., age forty-five, and Prof. Br., age thirty-five. Monday, May 26, 1918.

These cases were studied by Dr. D. L. Sisco, who reported as follows:

On May 26th Prof. Hu. and Prof. Br. ate, at the lunch club, the same experimental food, which was canned lobster, No. 1923. The same afternoon at about 4 o'clock, about three hours after eating the lobster, both developed rather severe headaches.

Prof. Hu. described his symptoms as follows: Headache, associated with malaise, both coming on about three hours after eating. There was no nausea or vomiting and no diarrhea. He had no abdominal pain, but complained of an "uncomfortable" sensation in the epigastric region. He could not sleep that night, due chiefly to the headache. Aspirin failed to relieve him and he eventually resorted to acetanilid. The headache persisted most of the next day, during which time he also says that he could "taste" the lobster. He took no cathartic and had no gastro-intestinal symptoms.

Prof. Br. describes his case as follows: "While eating the lobster I noticed a very peculiar, soapy taste, and very pronounced ammonia odor. I disliked the taste very much and did not finish what was on the plate. About one hour after lunch, and in spite of the room being filled with sunshine and warmth, the remnants of my lobster still gave off a very pronounced odor of ammonia mixed with another less definite odor. Toward 4 o'clock, about three hours after eating, I felt a dull headache coming on, which increased as time went on, so that I had to go home at 5 o'clock, not being able to do anything. I did not eat my dinner, took some salts, and went to bed. I was well the next morning."

An interesting speculation as to the cause of these symptoms is suggested in the fact that Dr. Hunt could "taste" the lobster throughout most of the next day. This leads one to feel that much of it might have remained in the stomach due to poor gastric digestion, a condition which might be explained by the neutralization of hydrochloric acid by the ammonia in the lobster.

Dr. Cheyney's examination of this lobster, can No. 1923, was entirely negative. He said that it appeared a little more moist than usual to him, but that there was no growth either aerobically or anaerobically, from any of his cultures. *The can of lobster had been incubated for one hundred and four days at 37° C.*

These are apparently cases of gastric indigestion without enteric symptoms, which seem undoubtedly due to canned lob-

ster which was shown to be sterile. There is little to incriminate the lobster other than an ammoniacal odor which it was noted to have, and that it appeared to be a little more moist than usual. There was perhaps some gastric stasis, but that does not seem necessary to explain the lingering taste of the lobster throughout the next day, for this might also be due to reversed peristalsis.

*Remarks.*—This particular can of lobster had been incubated at body temperature for over three months, and although no bacterial action took place, for the contents of the can was sterile, yet the lobster developed a pronounced taste and disagreeable odor.

CASE No. 10.—Dr. Mor. (Japanese), age thirty. Sunday, June 9, 1918.

At 9 A. M. had abdominal pain of a colicky nature, with restlessness, feeling of weakness, and dizziness. Pulse 72; constipation.

A bacteriologic examination of feces showed normal flora, mostly *Bacillus coli*; no pathogens.

*Experimental Food.*

June 7th—Salmon, can No. 769.

Incubated forty-three days at 37° C.

Bacteriologic examination—sterile.

Score—Normal taste, odor, and appearance.

Controls—Miss F. and Mr. A. ate contents of same can without ill effects.

Also—Blueberries, can No. 772.

Incubated twenty-two days at 37° C.

Bacteriologic examination—sterile.

Score—Normal taste, odor, and appearance.

Controls—Dr. I., Mr. Brn., and Mr. A. ate contents of same can without ill effects.

June 8th—No experimental food (Saturday).

*Remarks.*—This case was studied by Dr. Br., who diagnosed it intestinal indigestion (colic). Dr. Mo. thought that perhaps some fish cakes he ate at a restaurant Saturday might have been responsible. There was no evident relation to experimental food. (See also Case No. 1.)

CASE No. 11.—Miss Hus., age twenty-four. Monday, August 12, 1918, 8 P. M.

Sudden onset of diarrhea without any previous pains. Frequent loose movements Monday night and Tuesday. Tuesday night severe cramps and soreness of abdomen, which prevented much sleep. Wednesday morning (5.30 A. M.) profuse vomiting. Pains in abdomen persist. Otherwise no ill feeling. Rapid recovery.

*Experimental Food.*

August 12th—Salmon, can No. 1122.

Incubated forty-one days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in taste, odor, and appearance.

Controls—Miss C. and Miss K. ate contents of same can.

No ill effects.

*Remarks.*—Attack came on about seven hours after eating the salmon. No other experimental food eaten since Friday, August 9th, three days prior to the attack. Subject to gastrointestinal disturbances.

CASE No. 12.—Miss Gr., age twenty-two. Friday, September 13, 1918.

Illness began at midnight. Symptoms were mild and consisted of vomiting and abdominal pain. No diarrhea. Patient was tired out and overwrought nervously. Ate hearty meal and suffered from indigestion, according to physician who investigated the case. Prompt recovery.

*Experimental Food.*

September 11th—Beets, can No. 1264.

Incubated one day at 37° C.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—Miss K. ate contents of same can without ill effects.

Also—Pears, can No. 1267.

Incubated one day at 37° C.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—Miss Hus. and Miss Sp. ate contents of same can without ill effects.

September 12th—Chicken, can No. 1273.

Incubated seven days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—Miss Sp. ate contents of same can without ill effects.

Also—Apricots, can No. 1277.

Incubated two days at 37° C.

Bacteriologic examination—sterile.

Score—Normal in odor, taste, and appearance.

Controls—Miss Mo., Miss K., and Dr. Se. ate contents of same can without ill effects.

September 13th—No experimental luncheon.

*Remarks.*—It will be noted that no experimental food was eaten on the day of the attack, which was diagnosed "indigestion." Symptoms came on thirty-six hours after eating experimental chicken and apricots. Three other persons who had the same food suffered no ill effects.

CASE No. 13.—Mr. O., age twenty-two. Tuesday, June 17, 1919.

"Tuesday morning, June 17th, I arose at 5.30 A. M. feeling in usual good health. Breakfast at 6.30 consisted of oatmeal, toast, and coffee. Worked in the laboratory from 7.30 until 11 A. M. Lunch at restaurant consisted of roast beef, mashed potatoes, milk, bread, and cake. The morning was characterized by lack of energy. Food apparently good. Appetite good. During the afternoon had a marked tired feeling. At 6 P. M. had dinner at restaurant with Mr. Ar., which consisted of roast pork, apple sauce, mashed potatoes, milk, and bread. Walked back to the laboratory. Slight nausea, headache, very tired, absolutely no energy. Worked about one hour. Temperature 99.4° F. Had a movement of bowels at 9 A. M. That evening took a tablespoonful of Epsom salts.

"Wednesday morning headache gone; two movements of bowels that morning and one in afternoon. Stomach was unsettled, but appetite was good. At home Wednesday with more or less weakness and malaise."

*Remarks.*—Nothing in this attack was referable to anything eaten at the experimental lunch club.

CASE No. 14.—Mr. S., age twenty-eight. Thursday, June 26, 1919.

On Thursday, June 26th, Mr. S. was seized with rather severe abdominal cramps which were soon followed by a very loose movement of the bowels. There were no other symptoms except a slight feeling of indisposition and tiredness. Thursday night another loose movement was experienced. Friday morning found him feeling as well as ever.

This case was investigated by Dr. Dwight Sisco, who reported as follows:

During the last few days Mr. S. and Mr. Ar. have been eating practically the same food. For forty-eight hours previous to the onset of symptoms Mr. S.'s dietary was as follows:

Tuesday, June 24th—Breakfast: Orange, puffed wheat, milk, coffee.

Luncheon: Experimental, macaroni and cheese.

Dinner: Steak, potatoes, mince pie, coffee.

The steak was said to taste very old and was not very palatable.

Wednesday, June 25th—Breakfast: Same as Tuesday.

Luncheon: Experimental, tuna fish.

Dinner: Consommé, spaghetti with tomatoes, roast lamb with gravy, browned potato, canteloupe, coffee, apricot pie. Also two glasses of beer and one glass of root beer during the evening.

Thursday, June 26th—Breakfast: Same as Tuesday.

Luncheon: Experimental, frankfurters and potato salad.

Mr. Ar. ate all of this food with Mr. S. and Dr. Ch. part of it, and neither of them was affected in any way. None of the other members of the Lunch Club complained of trouble after eating the same lunches, so there seems no reason to blame them. As a matter of fact, there is little reason to feel that food was responsible for the trouble at all, for Tuesday, June 24th, was a very hot day and during that afternoon Mr. S. worked very hard, doing physical work of a nature entirely different from his ordinary work. Coupled with this was a certain nervous instability due to difficulties in his work, which had not progressed as smoothly as possible. It seems probable, then, that the

trouble was the result of three forces—nervousness, heat, and overexertion.

#### SUMMARY

An experimental lunch club was organized, with volunteers who ate the contents of 1750 cans of food that appeared of prime quality, but about 12 per cent. of these cans contained living micro-organisms. The tests extended over a period of sixteen months, and involved an average of 15 persons daily, who partook of the experimental food without cooking.

No ill effects whatever could be discovered as the result of the experiment. This seems reasonable when we remember that fresh food often contains myriads of living micro-organisms, in fact, we do not expect meat, milk, fruits, and salads to be sterile. By contrast, canned goods are the safest foods that come on our table on account of the processing to which they have been subjected.

(This work is a part of the investigation of food poisoning, conducted under the direction of Dr. M. J. Rosenau, Professor of Preventive Medicine and Hygiene, Harvard Medical School. The investigations are done under the auspices of the Advisory Committee of the National Research Council on the Toxicity of Preserved Foods, and under a grant to Harvard University from the National Canners' Association.)

## CLINIC OF DR. JAMES P. O'HARE

PETER BENT BRIGHAM HOSPITAL

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### VASCULAR HYPERTENSION

#### Report of 2 Cases, One with Autopsy

In this clinic I shall present 2 cases of vascular hypertension. This entity is characterized, as you know, by high blood-pressure with or without albumin and casts in the urine, but with a normal renal function. Evident arteriosclerosis may or may not be noted. It is, however, present in the older cases, at least in the smaller vessels, such as those of the retina. As a result of the progressive lesion in the vessels or the consequent secondary nutritional changes in the organs supplied by them death takes place in one of three ways: it occurs most commonly from cerebral hemorrhage, less commonly from angina pectoris or cardiac failure, and rarely from uremia. Now while death occurs in one of these ways, one must not think for an instant that the disease process in an individual case is confined to the brain, the heart, or the kidneys. The arteriosclerosis, while not at all uniform in its distribution, does not confine itself to any one group of vessels. Consequently, we find evidence during life—and postmortem—that many organs are affected. Consequently, our symptomatology and physical signs are very varied.

Our first patient is at present in the hospital with a cerebral hemorrhage. He has been an employee in the Medical School for the last fifteen years and, therefore, we have known much about him and have been able to keep him under observation for a considerable period of years. From 1911 to 1917 he was occasionally seen by two members of the Department of Medicine, and from 1917 up to the present time he has consulted me at frequent intervals. Furthermore, he has been a "house

"patient" in the hospital five times. As a result we have been able to follow with him the long road he has been taking, and make frequent observations of the progress of the disease.

When first he came to me in April, 1917, he was a married man of fifty-one, a stationary engineer. His chief complaint at that time was severe headache. The significant elements in his history follow.

In his *family history* we noted that his father had had a mild diabetes and died at fifty-six of cerebral hemorrhage. The latter is of especial interest, in that the majority of our cases of vascular hypertension show a family history of vascular, cardiac, or renal disease. In fact, it is one of the very few things one can put his finger on in attempting to get at the etiology of this process. The diabetes, too, is of interest as a possible element in his father's vascular lesion, and also because glycosuria was noted many times in slight traces in our patient. The only other element of importance in the family history is that for years he had been separated from his wife and family and had brooded much over it. This is of value because, of the few factors we recognize as bearing on the etiology, worry is one.

His *past history* includes the usual children's diseases and a Neisserian infection when a young man. It is surprising to find how little part past infections or even latent infectious foci play in this disease. This is true, too, of the effect of tea, coffee, tobacco, and alcohol. They do not seem to play much part. Our patient was a rather heavy smoker.

His occupation probably has been an important element in hastening the progress of the vascular lesion. His position for years has been one of great responsibility, which he has carried none too lightly. He has always worked hard either physically or mentally, or both.

You see, his history includes almost all the elements which seem to be of etiologic significance. He has been a hard-working, worrying man with a family history of vascular disease, holding down a very responsible position.

The first symptom referable to his vascular system was dizziness, noticed ten to fifteen years before he came to me in

1917. This has continued up to the present time, occurring almost every day for the last eight years. As long as he can remember he has had headaches, at least since 1907. While he does not remember clearly what they were like at first, they have been fairly characteristic during the last few years. They are frontal and occipital, and usually awaken him in the morning. As a rule, they have lasted about two hours. Of late they have been extremely severe and vise-like and of longer duration. This type of headache is fairly characteristic of the hypertensive case, whether it is just a pure hypertension or a chronic nephritis with hypertension. As a rule, it is occipital, either a pain or just pressure, and occurs only in the morning before getting out of bed. When the patient begins to whip up his circulation by getting up and around the ache disappears.

In 1910 our patient fainted and was unconscious for several minutes. He was told by his physician at that time that he had high blood-pressure. Just how high it was then we do not know, but we have records of his systolic pressure which the patient himself made when he was getting electric treatments late in 1914 and early in 1915. At this time the pressure was as high as 200 systolic.

In addition, the patient has always been nervous, more so of late. He has slept only fairly well. He has had occasional nocturia and, since 1915, was occasionally dyspneic on exertion.

When first seen by me in April, 1917, he was a somewhat fat, sallow man, rather depressed. His heart showed a very moderate hypertrophy. The peripheral arteries were not palpable. The arteries in the retina were "apparently not very abnormal," although the eye-grounds were not well seen at that time. The blood-pressure was 200/120. The urine was normal and the function of the kidney, as indicated by the excretion of phenolsulphonephthalein and the blood urea nitrogen, was normal. The former was 70 per cent. in two hours and ten minutes. The latter was 13 mgm. per 100 c.c.

In November of that year he was seen again, and there was essentially no change in his condition except that his headaches were less severe. This is of interest, in that some of these

patients have a period during which the headaches are extremely severe, and then later these become more bearable. The surprising thing is that during the later period the blood-pressure is higher than at the time when the headache was most severe. Accommodation of the cerebral circulation must account for this. The special renal test-diet at this time showed normal renal function. A finding of interest was that of glucose in the urine to the extent of 0.2 per cent. This has occurred intermittently ever since and is worthy of comment. It is a fairly common thing to note traces of sugar from time to time in this type of case. Whether or not arteriosclerotic pancreatic vessels are responsible I cannot say. However, I have performed the glucose tolerance test on a fairly large group of these cases, and find that most of them cannot handle sugar as well as normal patients, and they are not renal diabetics.

Our patient was not seen again till May, 1918, when he entered the hospital. This was necessitated by a profuse nose-bleed, lasting one hour, and severe enough to cause him to lose consciousness. He was compelled to stay in bed for two days. The bleeding apparently continued as a slight postnasal ooze, because he continued for three days to cough up blood which "had trickled down into his lungs." It almost seems unnecessary to state that one should always think of hypertension in epistaxis. And yet it was only a little earlier that one of our patients was admitted to the Nose and Throat Service of one of our big hospitals for nasal hemorrhage, and kept there for two weeks without having his pressure taken or the diagnosis considered.

At the time of entrance in May the patient whom we have been considering showed little change, except that his arteries were just palpable and his blood-pressure was higher—215/160. This diastolic is about as high as we ordinarily see it, although we have seen it around 170, and once 182. His urine, too, while showing no albumin, did show numerous hyaline casts. Bear in mind that casts and albumin do not mean nephritis. Furthermore, even when these two are accompanied by high pressure one cannot assume the presence of nephritis. One can only

assume that there is some renal damage and look for other evidence of nephritis.

Our patient stayed in the hospital for one week, during which his pressure dropped to 188/130. One must remember that marked falls and rises of pressure occur in vascular hypertension. These patients have a very sensitive vasomotor system, and variations in pressure are often sudden and marked. Of course, the systolic pressure is more variable than the diastolic, but the latter is not at all a fixed quantity. A fall of 30 mm. in systolic pressure is not at all uncommon after a rest of twenty to thirty minutes. Mental excitement of any kind or even moderate physical exertion may cause the systolic pressure to jump 30 to 40 mm. in a few minutes.

During this stay the renal function was found to be a low normal, and the glucose tolerance test showed some difficulty in handling glucose taken by mouth in a body weight dose. His Wassermann was negative.

The patient was seen occasionally during June and July because of two slight nosebleeds, nervousness, and apprehension. His headaches and dizziness continued. The blood-pressure continued to rise after leaving the hospital until it reached the level of 248/160. This is the usual story. Rest in bed causes a fall, but the pressure rises again on the resumption of daily life. The urine showed albumin for the first time and there were many hyaline and fine granular casts. Pulsus alternans also was noted for the first time. This important sign, you know, is characterized by alternate stronger and weaker heart-beats. It indicates a severe cardiac strain and is supposed to be of grave prognosis. And yet it has been noted more or less constantly in our patient for a year and a half. This sign is very easy of recognition. Of course, one can recognize it by polygraph tracings, occasionally by auscultation of the heart or by palpation of the pulse. But it is far more easily recognized by the auscultation method of taking the blood-pressure. In this, alternation shows itself in one of two ways. In the neighborhood of the systolic pressure either every other heart-beat comes through as a weak one or every other one fails to be heard until

the pressure in the cuff falls 20 or 30 mm. Another point of interest in connection with this sign is that in our cases it has always occurred with a high diastolic pressure, usually over 140.

About July 21st, after a long motor ride, our patient had another profuse nosebleed, and was admitted to the hospital for the second time. Examination at this time showed no change except that there was more evident sclerosis of the radial vessels. The pressure was 216/142. Renal function was practically the same except that the blood urea nitrogen was slightly above normal, 22 mgm., and the creatinin also was slightly higher, 3 mgm. Electrocardiograms showed no abnormality, not even a left-sided preponderance, which is characteristic of these hypertension cases with left ventricle hypertrophy. This at first seems rather strange, because clinically our patient had a very obvious cardiac enlargement. The explanation has been suggested by Lewis. He has found that in such cases, although the left ventricle is very definitely enlarged, both sides of the heart are enlarged in proportion. In fact, he has dissected out the ventricles and found that the relative weights of the two remain the same. The patient's stay in the hospital this time was essentially unimportant. The blood-pressure did fall somewhat.

Between the time of his discharge in July and his next entry into the hospital in November he was seen about half a dozen times. He was becoming very much discouraged about himself, and there was increasing evidence of a progressive process in the cerebral arteries. Nervousness and irritability had been increasing, and he noticed that his memory had begun to fail. In addition, there were other symptoms. He was "tired all the time" and complained of "sciatica." These two are worthy of comment. Tire is very characteristic of this type of case. Almost every one of these patients complains of this symptom. As a rule, they are capable of a supreme effort for a moment, but they are quickly exhausted. They cannot persist. They have been well spoken of as "dash men" rather than as "long distance runners." This is illustrated in another way in our patient. At this time he took a vacation of three weeks, and returned feeling very well. He buckled down to his old work

with a good deal of vim, but in a very short time all of his symptoms returned. The "sciatica" mentioned above did not seem to me at that time to be a true sciatica, but one of those rather indefinite pains that are so common in these patients. Many of them complain of all sorts of vague back pains and pains in the extremities. It is very difficult to give the "raison d'être" for these various pains, but they are probably circulatory and related closely to the muscle cramps, which are extremely common in vascular hypertension.

The general condition of our patient remained about the same and urinalysis showed no change. The blood-pressure had climbed a little and he was beginning to get up once or twice every night.

During the fall of 1918 he was doing fairly well, until early in November, when he had an automobile accident. He was very badly upset by this and became extremely nervous. The headache and dizziness grew very much worse. A new symptom, too, was noted at this time—transient blurring of sight lasting a minute or two perhaps. This was undoubtedly due to temporary spasm of the retinal vessels. Spasm of the arteries in vascular hypertension is fairly common. It explains many of the cerebral attacks that at first suggest hemorrhage. It has actually been observed appearing and disappearing in the retinal vessels.

The systolic and diastolic pressure of our patient had risen (246/154). Pulsus alternans continued and extrasystoles were noted in the heart. The patient had himself recognized these by the sudden "jumps" taken by the heart from time to time. These "jumps" were undoubtedly the strong contractions occurring after the long pause which frequently follows extrasystoles.

On November 14th he entered the hospital for the third time because of increased nervousness, higher pressure, and a slight nosebleed. Examination at this time showed that the heart was increasing in size. The peripheral arteries were apparently about the same, but changes were evident in the retinal arteries. These showed beginning signs of arteriosclerosis. In

addition, there were two white spots, probably degenerative, in the retina. It may not be amiss to say a word here about the retinal vessels. The signs of sclerosis in these are numerous, but the important ones are pressure effects of artery on vein, where they cross each other, and unevenness and irregularity of the lumen of the vessel. The pressure effect of artery on vein may be merely slight mounding up of the vein over the artery or "nicking" of the vein by the superimposed artery. Where the artery is more sclerosed, the vein may be bent out of its course. In marked cases the vein may be considerably bent around the artery, and its lumen may not be seen for a considerable space on either side of the superimposed artery. Less important signs of arteriosclerosis are "sheathing" of the vessels, widening of the central light streak, narrowing and stiffening of the vessels, and increased tortuosity. By "sheathing" is meant merely that the vessel wall is no longer transparent and may be seen as a pinkish-white streak on either side of the column of blood. It should not be forgotten that what one sees in looking at a normal retina is not the blood-vessels themselves, but merely the blood in the lumen. The walls are transparent. As a result of sclerotic processes developing in these vessels the walls may become more and more opaque, so that eventually even the blood column may no longer be seen, but the vessel represented by a whitish cord in whole or in part. "Unevenness" is indicated by irregular narrowing of the blood column. "Widening of the central light streak" seems to me to be of very little value in determining the degree of arteriosclerosis. "Increased tortuosity" has about the same significance, unless it is the very small vessels that have taken on the "corkscrew" characteristics.

In addition to the signs in the vessels the retina in such a case as ours should be watched for white spots of degeneration and hemorrhages. Exudate may be present, but is by no means as conspicuous as in the chronic nephritic with hypertension.

At this entry our patient's urine was practically the same, except that the amount of albumin had increased. A slight trace of sugar was again found. The functional tests were normal, showing that the process in the kidney was remaining

within the renal vessels and had not yet caused any lasting damage to the functioning parenchyma.

During his one week stay in the hospital the blood-pressure fell to 210/140. The patient's confidence returned somewhat, but otherwise there was not much change. Alternation of the pulse was continuously present, but there was absolutely no change in the electrocardiograms to indicate any progressive myocarditis. This would be characterized by a gradual spreading of the curve representing the ventricular complex.

After leaving the hospital our patient seemed to be considerably better for a while. He slept well and had much better control for some time. Cramps in his legs bothered him somewhat. Dyspnea on exertion reappeared, and the sharp precordial pain which he had noticed previous to his last entry returned. It is noteworthy that the *pulsus alternans* disappeared when the diastolic pressure dropped to 127, and that it reappeared when the pressure again rose to 142. This tends to confirm my impression that this alternation is closely associated with a high diastolic pressure. This does not mean that all high diastolic pressures are accompanied by *pulsus alternans*. On the other hand, in my group of hypertension cases this phenomenon has only occurred when the diastolic pressure is 140 or higher.

Let us return to our patient. A short vacation helped to bolster him up at just the time when he began to slip. In December, however, labor troubles in his plant upset him greatly, and his nervousness and sleeplessness returned. With this the blood-pressure rose, reaching 240/148. Precordial pain increased and came on occasionally without any apparent exertion. Examination of his heart at this time showed extrasystoles. Retinal examination showed but little change, except that the vessels seemed more straight and stiff and there were a few white spots of degeneration.

Just after Christmas one of the cerebral accidents which we had long been expecting occurred. On the night of December 26th the patient was awakened by a severe headache. On arising early the next morning slight ataxia was evident. He noticed that he could not button his clothes well and that when

he wished to step up he had some difficulty in placing his feet. He walked over to the hospital to see me, and it was evident there was slight ataxia involving chiefly the left side. There was no other evidence of cerebral trouble. The blood-pressure was still high, but not higher than it had been previously. Our impression at that time was that the patient did not have a hemorrhage, but a mild vascular crisis, a spasm of one of the cerebral vessels, with perhaps some perivascular edema.

On the morning of December 28th he awoke "feeling very badly." Just what sensations he had we have not been able to find out because he does not remember clearly what happened at that time. He was just able to telephone for help and then apparently fell. Whether he had a convulsion or not it is rather difficult to decide. When found he was partially conscious, but unable to speak. His tongue had been bitten. This, of course, is in favor of the convulsion theory. On the other hand, the wound may have been produced by his fall. He became fully conscious about three-quarters of an hour later and complained of a very severe headache and numbness in his left arm. The latter probably was due to local injury resulting from the fall in view of the findings made shortly afterward in the hospital. He was admitted immediately.

At entrance he was perfectly conscious. There were no signs of paralysis except a slight suggestion of weakness of the right side of the face. There was, in addition, slight ataxia of the left hand. It is very difficult to differentiate here between cerebral hemorrhage and cerebral vascular spasm. Either might account for the sudden explosion. The fact that such a violent explosion occurred without leaving any greater residual paralysis, and the fact that it cleared up so quickly, points toward vascular spasm rather than hemorrhage. Had a hemorrhage occurred in the silent areas of the brain—the frontal convolutions—we should not expect so rapid a recovery of consciousness. Furthermore, there was some evidence—slight indeed—of a localizing lesion outside of these silent areas.

Examination of the heart showed that it was continuing to increase in size, the left border being now  $13\frac{1}{2}$  cm. from mid-

sternum. The blood-pressure was lower, 202/134. It is not uncommon after any cerebral attack to find the blood-pressure lower than it has previously been. In our patient the pressure continued to drop, reaching on that same day 180/120. An interesting but rather alarming observation was made at this point on the effect of bleeding. I had left instructions to have the patient bled. When the house officer got around to do this the pressure had reached the low figure given above. Bleeding, of course, with such a falling pressure was no longer indicated. In spite of this, however, the man was bled copiously. As a result he went into partial collapse, became very pale, and was bathed in a cold sweat. His blood-pressure at this stage was found to be 90 systolic and 70 diastolic—quite a drop from 202/134. Readings were taken at frequent intervals during the next twenty-four hours, and at the end of that time the pressure was back again at 220/140.

Two days after this attack there was practically no evidence that there had been any disturbance except that the slight ataxia of the left hand persisted for a short time. The patient stayed in the hospital for two weeks or more, during which his blood-pressure fell to 170/130. This was while he was in bed at rest. As soon as he began to get up and around it rose again to 210/140. This is the usual story. The phthalein excretion and the blood urea nitrogen showed that the kidneys were still functioning normally. Glucose was again found in the urine.

During the early part of 1919 there was but little change in the general condition of the patient except that the symptoms indicating increased involvement of the cerebral vessels were becoming more evident. He became more and more nervous and very sleepless. His memory, too, began to fail and he became very melancholic. Dizziness was almost constant and was made very much worse by smoking even a single cigarette. The severe headache returned, and the patient noticed that it was very much worse whenever he ate more than he should.

The cardiac side of the picture did not change much. Dyspnea of slight degree continued and there was occasionally dull pain under the sternum and some precordial tenderness. The

blood-pressure gradually rose, especially the diastolic. Early in February the systolic was 256 and the diastolic 172. This is an extremely high diastolic and a distinct rarity. In March the pressure varied between 210 and 242 systolic, 140 and 156 diastolic. Urinalysis showed no change, and the functional tests in January and March were essentially normal.

The cerebral sclerosis continued to advance. In April he reported that he was much more irritable and that it was much harder for him to concentrate. He worried greatly about himself and seemed always to be expecting the cerebral hemorrhage "which he knew was going to kill him."

A new cardiac symptom developed at this time. This was an occasional sudden attack of dyspnea coming on apparently without exertion or known cause, and lasting about a minute. These attacks of paroxysmal smothering are akin to and often associated with angina pectoris. There is often, too, a feeling of tightness, as in angina, referred to the base of the heart. Examination of the heart in this case showed no change. Extrasystoles were occasionally heard.

Shortly after the middle of April another cerebral explosion occurred. On the night of the 19th of April he was awakened out of a sound sleep. He first noted a feeling of numbness and then tingling of the left hand. Then the hand seemed to contract and he could not straighten it. These symptoms quickly spread to the right hand, and immediately afterward he had a generalized epileptiform convulsion which seemed to be more marked on the left side. It lasted about ten minutes, according to friends. He then woke up and talked clearly. Apart from a headache and a slightly dazed feeling he was apparently all right when I saw him about half an hour later. There was no evident paralysis. The heart showed a gallop rhythm and the blood-pressure was 206/124. Here again we note a fall in pressure after a cerebral crisis. For the same reasons given above we regarded this attack as probably a vascular spasm. The explosion was sudden, the attack was over in a very short time, and there was no paralysis.

Retinal examination within a few days showed that the ar-

teriosclerotic process in the vessels was advancing by leaps and bounds. In addition, there was some edema of the disks, and in one eye a small linear hemorrhage and a small white patch of exudate. This is the first hemorrhage noted in the eye-grounds, and probably occurred during the convulsion. The exudate, too, was a new finding. "White spots" had been previously noted, but these were probably spots of degeneration rather than true exudate.

During the following summer there was a gradual, rather sad, change in the patient's mental faculties. He became very much depressed. Everything seemed hazy to him. His memory continued to fail and he had the greatest difficulty in concentrating on anything. Co-ordination of the movements of both hands even seemed to be impaired. Confidence in himself was lost and he was always "afraid of making mistakes." The picture was truly a pitiful one, made more so because the man was intelligent enough to know what was going on and what the outcome was to be.

In the early fall these symptoms gradually increased. About the middle of September he had another attack which may or may not have been cerebral. It was very slight and was characterized merely by being awakened from sleep by a "peculiar feeling," as if he were going to lose his mind. It passed off shortly, but disturbed him greatly.

The heart in the meantime continued to enlarge, and there was evidently an increase in the supraventricular dulness. A 6-foot x-ray plate confirmed the enlargement of the heart and showed a diffuse dilatation of the arch of the aorta. A systolic gallop rhythm was almost constant. Pulsus alternans was present continuously. The blood-pressure showed the usual variations. The retina showed an extreme degree of arteriosclerosis, a fresh hemorrhage, and some white spots of degeneration in one eye. There were no changes in the urine.

On October 19th, after a week of increased physical and mental effort, he was about to leave his home when he complained of a peculiar sensation in his head. His speech immediately became thick and he lapsed into a condition of semi-

consciousness. It was possible to arouse him, but he could not speak. For a short while he seemed to recognize those who came into his room. When I saw him, within an hour, he failed to recognize me. His systolic pressure was 260, and there was a very evident complete right-sided paralysis. The next morning we sent him into the hospital.

At entrance his condition was about the same. The heart seemed to have been getting progressively larger. The peripheral arteries were palpable and tortuous. The blood-pressure had dropped to 230/140. There seemed to be a complete right-sided paralysis. Patient was semiconscious. Reflexes were all active, but those on the right seemed greater than those on the left. Urine showed considerable albumin, which is usual after any attack of unconsciousness. The blood urea nitrogen was 20 mgm. per 100 c.c. The creatinin was 2 mgm. per 100 c.c.

During the two days following his entrance into the hospital consciousness returned. He tried to speak and answer questions, but was unable to do more than mumble inarticulate sounds. The right arm and leg could not be used. On the second day the systolic pressure rose to the high level of 278. The diastolic remained at 140.

During the following week his condition improved somewhat, although it must be said that this was not steady. One day he would seem well, and the next day not so well. He had at times some difficulty in recognizing the people around him. At other times he was perfectly cognizant of his surroundings. He was, however, unable to speak to friends or call them by name. His speech was very thick and he was unable to use the words he wished to use. At times he seemed to realize this fact. The power to use the right side of his body returned, so that at the end of this week there was no evidence of the former hemiplegia except a little right-sided weakness of his face and of the grip. During this time the systolic blood-pressure varied from 250 to 190; the diastolic, from 174 to 130.

The next three weeks showed a gradual improvement in the patient. Apart from the right side of the face, which still showed weakness, there was no evidence of the involvement of

the right arm and leg. His mentality, which seemed more or less clouded since the attack, cleared considerably. He recognized almost everybody that came to see him, and after a while could speak the names of those he knew best. Names of recent acquaintances he had great difficulty in remembering. His speech, which had been thick, improved, so that the words he used were fairly clearly spoken. However, he showed much confusion in his speech, the words used not being the words he tried to use. Occasionally he seemed to be aware of this fact. For example, when asked how he felt, he might reply, "Yes, indeed, the bed in." He no longer had the apparent motor aphasia of the early days after the attack, but a definite sensory aphasia or word-blindness. As time went on this improved too. He might answer a few questions fairly successfully. But he tired quickly, and then the answers became badly jumbled words.

There has been steady but very slow improvement in his mental condition up to the present time. His general condition now is as good as it was before the last attack. Physical examination today (November 22d) shows slight right-sided weakness of the face. The tongue protrudes straight in the midline. There is a moderate pulsation in the vessels of the neck and in the suprasternal fossa. Radials and brachials show more thickening and tortuosity than before, but there is no calcification or beading. The pulse volume is moderate and pulsus alternans—which yesterday was easily made out by palpation of the radial—is just suggestive. It is, however, quite evident when taking the blood-pressure. The latter is 204 systolic, 142 diastolic. This is somewhat higher than it has been during the last few days.

The apex impulse of the heart was somewhat diffusely felt in the fourth and fifth space, the point of maximum intensity being in the fourth space, 12.5 cm. from midsternum. The left border of dulness measures 13 cm. from midsternum, the right border, 3.8 cm. The supracardiac dulness in the second space is 7.5 cm. No thrills are made out. The heart is regular and the rate is slightly increased. This is more evident when the patient sits up, the exertion causing a considerable rise in heart rate. The first and second sounds are somewhat alike except at the

base, where the second sounds are accentuated. A systolic gallop rhythm is just suggested at the base. There are no murmurs.

There is no evidence of the hemiplegia as far as the ability to use the arms and legs is concerned. Both knee-jerks and ankle-jerks are hyperactive and equal. All of the reflexes in the right arm are somewhat more active than on the left. There is no Babinski or ankle-clonus.

Examination of the eye-grounds is of considerable interest. Arteriosclerosis has increased markedly in both eyes. The right eye shows nothing else. The left eye, however, shows, in addition, a marked optic neuritis with some edema of the retina around the disk and a few spots of exudate. There is no hemorrhage. The interest lies in the fact that the optic neuritis is unilateral and corresponds to the side of the cerebral lesion.

The urinalyses and renal function tests show that the kidneys are still acting normally.

Dr. McPherson, who is very much interested in the neurologic side of this case, contributes the following information about the aphasia: There is marked disturbance of spontaneous speech. This means that the patient is absolutely unable to keep up a conversation. Serial speech, however, is fairly well preserved. The patient is quite able to say combined sentences. Repetition, too, of sentences spoken to him is fairly easy. He is absolutely unable to read or write spontaneously. There is some doubt about his ability to write to dictation. Copying has not been tried. Except for simple commands, his understanding of speech is practically lost. Analysis of the above findings brings this case into the group of "complex aphasias." It is essentially sensory, and the lesion was probably a hemorrhage of the parietotemporal branch of the midcerebral artery. The lesion originally extended forward to the motor area, causing hemiplegia. The area now involved is largely Wernicke's zone, together with a small area just posterior to this zone.

The prognosis in this case is undoubtedly very poor, although I am inclined to think that the patient's mental condition will clear considerably. The arteriosclerotic process, however, has been developing with such marked speed during our observation

that he will, without question, die from another cerebral hemorrhage. Treatment, except for symptoms, will not help to any extent. Everything in the way of diet, drugs, etc., has been tried without avail.

The second case illustrates the rare mode of death in cases of vascular hypertension—from renal insufficiency and uremia. We occasionally see—for the first time—cases of chronic nephritis with somewhat depressed function which seem to have started as pure vascular hypertension cases. We very rarely see such a case, however, while it is still a purely vascular condition with normal renal function, etc.; and then follow it while the vascular disease causes progressive destruction of renal parenchyma and consequent renal insufficiency, uremia, and death. We have had the good fortune to have 2 such cases—one of which is the following:

This patient is a man of thirty-five, who had had numerous infections in childhood and syphilis at twenty-five. His childhood infections consisted of pneumonia with empyema, chronic bronchitis and asthma, scarlet fever, trauma, with resultant cataract. He had had absolutely no symptoms referable to his cardiac, renal, or vascular system until two weeks before his first entry into the hospital, June 13, 1917. At that time he had a "cold." On the night of June 2d he had severe paroxysms of coughing, and on awakening in the morning noticed that his vision in his good eye (the other had a traumatic cataract) was much blurred. He was slightly dyspneic. His oculist sent him to a physician, who found a positive Wassermann and sent him to the hospital for treatment.

Physical examination disclosed a marked general arteriosclerosis; a hypertension of 250/150; and a considerable cardiac hypertrophy, left border being 12 cm. from midsternum. There was much hemorrhage, exudate, and arteriosclerosis in his good eye. His urine showed an ability to concentrate; only the slightest possible trace of albumin; and a rare cast. Functional tests were all practically normal, except that the two-hour renal test showed a slightly increased night volume, with a lowered specific gravity.

His one month's stay in the hospital was rather uneventful. His urine continued to show a very little albumin and a very rare cast. The specific gravity was normal. His blood-pressure fell considerably—to 180/120. His phthalein excretion fell off slightly. There was some improvement in his sight and he was discharged "improved" on July 14, 1917.

We can reason that, as a result of his syphilis, he had had a marked arteriosclerosis and an unrecognized hypertension for some time. His paroxysms of coughing raised his blood-pressure, with resultant retinal hemorrhages and cardiac dyspnea. His kidneys at this time were essentially normal.

During the nine months previous to his next entry into the hospital he slowly developed increased vascular and cardiac symptoms—dizziness, occipital morning headaches, considerable dyspnea, and angina. Renal symptoms, except nocturia, were lacking. His urine showed no change and his functional tests were even more normal. His blood-pressure gradually rose to its former high level—240/150. He then came into the hospital for study on April 13, 1918.

Examination at this time showed his general condition much worse. The heart and vessels were about the same. The blood-pressure was very high. His eye was somewhat improved. The urine for the first time showed evidence of an active breakdown of kidney substance and his renal function had begun to fall. Evidently at this time the condition had already progressed from a pure arteriosclerosis into the class of true nephritis.

Inasmuch as he was not improving, he was given three small doses of diarsenol. As far as could be seen this treatment only caused greater activity in the kidney, and his renal function continued to drop. Part of this treatment was given during his stay in the hospital, and the rest after his discharge on April 27th. He returned to the hospital for this treatment.

Soon after his last treatment he developed a sharp pain in his right upper quadrant, for which he entered the hospital again on May 24th.

Physical examination at this time showed a rapid, steady decline in the patient's condition. He had lost much weight

and strength. A pleurisy accounted for his pain. His blood-pressure was very high, especially his diastolic, which had climbed to over 170. The heart had enlarged perceptibly and was not perfectly compensated, as indicated by the crackles in his lungs and by the liver, which was enlarged and tender. The urine showed much greater activity. The phthalein excretion was just a little below normal and his blood urea nitrogen had begun to climb above normal. The retina showed considerable improvement, but also a fresh hemorrhage and some exudate.

In the hospital there was no change, except a slight one for the better in his vision and general condition. He was discharged on June 10th.

This improvement lasted only two weeks. He then began to have severe cardiac symptoms, nocturnal dyspnea, smothering, and orthopnea. More significant than these was the appearance of definite renal symptoms—twitching of arms and legs, marked nausea, and vomiting. Venesection of a large amount of blood was done, and the nausea and vomiting ceased. The dyspnea and twitchings, however, continued, and he returned to the hospital on July 6th.

Examination showed his general condition obviously much worse, but with nothing actually new. The blood-pressure was about the same. The retina had improved somewhat, showing no new hemorrhage and no exudate, but only a blurring of the disk and old choroidal pigment spots. The urine showed greater activity. His phthalein had dropped to 0, and his blood urea nitrogen had risen somewhat—to 47 mgm.

At this time, therefore, there was a definite uremia in addition to the cardiovascular disturbance.

In the hospital he grew rapidly worse. He became very drowsy and irrational. Exophthalmos developed in the last four days. The twitchings became more marked, as did the dyspnea. He finally developed Cheyne-Stokes' respiration. He died just after his first general convulsion on July 17th.

In the meantime his blood-pressure and blood urea nitrogen had climbed moderately. It is of interest to note that the diastolic reached the high level of 182, the highest I have ever seen;

also that although he died presumably in uremia, his blood urea nitrogen was only 53 mgm. The cardiac and vascular apparatus was playing a very important part.

Autopsy disclosed the fact that the kidneys were small. The right weighed only 110 grams, and the left 140 grams. They were deep red in color, with a finely granular surface. There was found a cortical cyst in the right lower pole. The cortex was thin, averaging 4 mm. in width. Microscopically, the arteries and arterioles showed all stages of sclerosis, from slight thickening of intima to complete obliteration, with occasionally a hyaline thrombus in the constricted lumen. The glomeruli showed changes of all sorts. Many were normal. In others there was marked congestion of the capillary tufts and swelling of the endothelium lining the capillaries. Hyaline thrombi were present in many of the glomeruli and many tufts were entirely converted into compact masses covered with epithelium. The capsule was often thickened and the tuft adherent to the capsule. There was considerable dilatation and distention of the remaining convoluted tubules by albuminous fluid. Hyaline casts were present in a few of the convoluted and collecting tubules. There was some increase in stroma, more marked in some spots than in others.

The kidney, in brief, showed rather marked changes of chronic vascular nephritis.

Here, then, is presented a case of syphilitic vascular disease which, when seen at the onset of symptoms, showed only vascular hypertension and essentially normal renal function. During the next ten months the functional tests disclosed no renal insufficiency. Without doubt the vascular disease within the kidney was progressing during this time. In the next three months, however, renal insufficiency appeared. The function fell to 0, and death occurred in uremia.

The 2 cases of vascular hypertension here presented illustrate most clearly two distinct paths which such cases may follow. One is the road leading to cerebral hemorrhage and, barring intercurrent disease, death from another such cerebral accident. The other leads to destruction of renal tissue, renal insufficiency, uremia, and death.

## CLINIC OF DR. C. W. McCLURE

PETER BENT BRIGHAM HOSPITAL

### GOUT

#### A Report of 13 Cases with Tophi, and Remarks on the Symptomatology, Metabolism, and Therapy

THERE is but one universally accepted pathognomonic evidence of gout, and that is the tophus. An accurate symptomatology of gout, can, therefore, be obtained only from observations made on patients in whom tophi have been demonstrated. Following this rule the data on gout which have been collected in the Clinic of the Peter Bent Brigham Hospital are portrayed in the following 13 cases. All of these patients were studied in the hospital wards. For the sake of brevity the complete data collected will not be given, but only findings which were positive.

CASE I.—J. G., Med. Nos. 5421, 6320, 6853. White, male, butcher, aged fifty-eight. Admitted to Peter Bent Brigham Hospital October 10, 1916, and discharged improved November 7, 1916.

**Diagnosis.**—Gout; chronic arthritis; hypertension; arteriosclerosis; chronic myocarditis.

There was no family history of gout or arthritis. Before the first attack of arthritis, twenty-five years ago, the patient drank beer freely (8 to 10 glasses per day). He was raised in Wirtschaft, Germany, and drank beer from early childhood. He used neither wine nor whisky. He was a butcher and sausage maker and ate freely of meats. The distal two phalanges of the right forefinger were amputated in a sausage machine twenty-one years ago. During the past few months there had been

occasionally palpitation, with some shortness of breath on exertion.

**Arthritic History.**—Twenty-five years ago there occurred an attack of polyarthritis, diagnosed by several physicians as "acute rheumatism." While walking to work the patient was seized suddenly with agonizing pain in both hip-joints. He got back to his house with difficulty, although when the pain seized him he was only a block and a half away. Every step was painful. He was obliged to climb up the stairs to his flat on hands and knees. He was crying aloud with the pain, which remained so severe for the ensuing five weeks that sleep was impossible. After the first few days the inflammation left the hips and attacked the knees, which became enormously swollen (in describing the size the patient put his hands a foot apart). The skin became red "like fire," tense, and so tender that the bed sheet felt "so heavy that it made him holler." Later the whole of both feet and all the toes became swollen and painful; the big toes were no more involved than the other toes. Later in this same attack the hands, wrists, elbows, and shoulders became swollen and painful. Three or four joints were sometimes involved contemporaneously. Every motion of the body was painful and for weeks he was unable to feed himself. The face was so swollen that his eyes were closed for several days. The fever was high and there were some sweats. At the end of six weeks he was taken to the Boston City Hospital, where he remained ten weeks. Four years later a second attack of arthritis occurred. It began in the right great toe and later involved the knees. The affected joints were numb, swollen, "red as blood," and "shiny." This attack was diagnosed as gout. For the past sixteen years attacks have occurred almost every winter, lasting two to three months, and usually confining him to bed. At some time or other during these attacks all the joints have been involved, including those of the cervical vertebrae. Every few days, during an attack, the inflammation would shift from one joint to another. The skin over the affected joints often peeled off after an attack. A few years ago the olecranon bursa swelled, "forming bundles the size of small hen's eggs." About six months

later these swellings disappeared. During the past five years the intervals between attacks have been of only a few months' duration. In the interim between attacks there were times when joint pain, of severity sufficiently marked to prevent sleeping, occurred. In the winter of 1915 the temporomandibular joints were exquisitely tender and painful during an attack of acute arthritis.

During the damp weather more or less joint pain was frequently present; similar to the type of pain occurring in the ordinary varieties of chronic arthritis.

**Physical Examination.**—The patient was a well-developed, very obese man. Just in front of the lower portion of each ear there was a soft, large, fluctuant swelling (tophi). These were said to be extremely painful during the attacks of arthritis. There was some increase of fluid in both temporomandibular articulations. There were small tophi in each ear. The area of relative cardiac dulness measured 14 cm. to the right and 3 cm. to the left of the midsternal line. The heart rate was regular. The aortic second sound was accentuated. There were no murmurs. The walls of the radial arteries were markedly sclerosed. Blood-pressure was 185 mm. systolic and 117 mm. diastolic.

**Extremities and Joints.**—The hands were thick, heavy, and much scarred by old cuts. The fingers of both hands were more or less stiff, especially the first interphalangeal joints. The patient could not clench his fist. The soft tissues about the finger joints were much thickened. On several of the fingers, near the joints, were soft, fluctuant, nodular swellings. The skin over these swellings was smooth, glistening, and slightly reddened. Motion of both wrists was limited, flexion being moderate and extension very slight. Adduction and abduction were almost impossible. Some crepitus was palpable on motion of the wrist-joints. The elbow-joints could not be fully extended and crepitus was palpable on motion. The shoulder-joints were normal. There was slight crepitation in the hip-joints on rotating the thighs, but there was very little limitation of motion. Neither knee could be fully extended. The periarticular tissues

were thickened. Motion produced marked crepitus. There was diffuse thickening of the left tibia and some irregularity about the site of a former fracture. The periarticular tissues of the ankle-joints were thickened, and the joints showed limitation of motion. The toes were not much deformed except for marked double hallux valgus.

The patient had noticed the nodular tophi on the fingers for about three years.

**Summary of the Radiographic Findings.**—The changes found were atrophic, proliferative, and destructive in type. Certain bones and their joint surfaces were involved in these changes, while others were normal or nearly normal. Some of the joint spaces were obliterated and ankylosis had occurred in certain of them. There was partial subluxation of one joint. There were focal areas of decreased density in some of the bones. The regions in which these areas occurred usually showed other bony changes. Nodular thickening of the soft tissues and arteriosclerosis of the larger vessels were present.

**Clinical Pathology.**—*Urine.*—Examinations of the urine at all times gave no abnormal findings. Phthalein excretion was 53 per cent. in 1916 and 47 per cent. in 1917. The two-hour renal test showed nothing definitely abnormal.

*Blood.*—Hemoglobin was 100 per cent. White cells were 7000 per c.mm. In 1916 urea nitrogen was 11 mgm., non-protein nitrogen 38 mgm., and uric acid from 4 to 5 mgm. per 100 c.c. of blood. In 1917 urea nitrogen was 14 mgm. per 100 c.c. of blood. In 1919 non-protein nitrogen was 44 mgm. and uric acid 9 mgm. per 100 c.c. of blood. Wassermann reaction in the blood-serum was negative.

Sodium urate crystals were demonstrated in specimens obtained from tophi in the ears and on the fingers.

Basal metabolism, determined by indirect calorimetry and calculated according to the linear formula of DuBois, was 90 per cent.

**Progress.**—During his stay in the hospital the patient had an acute gouty arthritis of fourteen days' duration. The attack began with constant, sharp, needle-like pains in the metatarso-

phalangeal joint of the right hallux. The joint became swollen, scarlet red in color, hot, and very tender. After two days the dorsum of the right foot became similarly affected and pain was present in the tendo achillis on motion. After a few days the pain subsided in the right great toe and foot, and at the end of ten days from the onset of the attack were again normal. Coincidently with the subsidence of pain in the right foot a typical attack of podagra affected the left great toe, the first and second metacarpophalangeal joints of the left hand became painful and tender, and pain on motion was present in the right knee, the left knee, the left wrist, and both shoulder-joints. Within the ensuing forty-eight hours the left great toe joint, the terminal joint of the third toe of the left foot, left knee, all metacarpophalangeal joints, the second joint of the third finger of the left hand, and the right wrist and elbow were swollen, scarlet red in color, tender, hot, and constantly very painful. The patient was then given wine of colchicum and within the next two days all symptoms subsided.

During the gouty attack the temperature gradually rose to 103° F. and then dropped to normal within forty-eight hours after the administration of wine of colchicum. The pulse-rate was slightly accelerated, varying between 80 and 90 per minute.

During his stay in the hospital the blood-pressure dropped to 140 mm. systolic and to 68 mm. diastolic. The blood-pressure recorded in March and June, 1917, was 200 mm. systolic and 105 mm. diastolic. During the interim between admissions the patient had frequent onsets of gouty arthritis. He was able to quickly control these attacks by the use of wine of colchicum, and in this manner led a comfortable life.

**CASE II.**—A. L. E., Med. Nos. 1050, 1120, 4166, 5297. White, male, carpenter, aged forty-eight. Admitted to the Peter Bent Brigham Hospital September 14, 1916, and discharged improved December 4, 1916.

**Diagnosis.**—Gout, acute and chronic; chronic arthritis; cirrhosis of the liver; purpura; alcoholism, chronic; chronic nephritis.

The father was killed accidentally. The mother died of "shock." For twenty years the patient had drunk 3 to 10 whiskies and 3 to 10 glasses of beer a day.

**Arthritic History.**—Three years before the first admission, in 1914, there had been a slight attack of "rheumatism" in the patient's elbow and shoulder, which had persisted three days. In 1912 an acute attack of arthritis involved the wrists and fingers. These were red, swollen, and excruciatingly painful on motion. In subsequent attacks prior to 1914 the elbows, knees, and ankles had been similarly affected. On admission to the hospital in 1914 the proximal joint of the right middle finger was swollen and slightly painful on motion. Both knee-joints contained fluid, were much swollen and markedly painful on motion, but were not reddened. The left ankle, the dorsum of the left foot, and the left great toe were swollen, red, and exquisitely tender. The right ankle was moderately swollen and painful on motion, but not red and not very tender. On the inner surface of the right large toe was a swollen reddened area which was very tender and painful. Within a few days the arthritic symptoms had largely subsided due to the administration of atophan. Within a week all acute gouty manifestations had disappeared and the patient was discharged. One week after discharge he was readmitted to the hospital for another gouty attack. The left knee was somewhat swollen, but contained no demonstrable fluid. Just below the inner side of the left patella was a small, circular, red, and exquisitely tender area. The left ankle was considerably swollen, bright red, and very painful. Within a few days the arthritic signs had completely disappeared under the administration of atophan. He was discharged in May, 1914, and readmitted February, 1916. In the interim he had had no joint trouble except for a little indefinite pain in both feet during rainy days. He had had rather frequent painful cramps in the muscles of the calves, thighs, arms, and neck. The arthritic attacks were accompanied by fever of from 100° to 101° F.

The patient was admitted with the following history: "Last Sunday night he went to bed at 11 P. M. feeling well. The next

morning (yesterday) when he attempted to step on the floor he had a sharp attack of pain in his left foot, especially in his great toe and ankle, and he could not stand on it. The foot was reddened and very tender, but was not swollen. The pain was particularly severe when he attempted to flex it, and he was compelled to sit down all day. He could not sleep last night because of the pain and the muscle cramps in his legs, which became very severe. This morning the foot became swollen and the left knee reddened and painful on motion. He also noticed, this morning, pain on bending his left wrist. No other joints have been involved." On physical examination the left ankle and dorsum of the foot were swollen, reddened, hot and painful to touch or passive motion. The tenderness was particularly marked about the base of the left great toe. There was marked tenderness about the left knee-joint and sharp pain on passive motion.

**Present Illness.**—The patient was admitted to the hospital because of purpura. Since the last admission (February, 1916) he had had, occasionally, slight pains in his joints. Otherwise there had been no arthritic manifestations.

**Physical Examination.**—The patient was a well-developed, well-nourished man. Mentally he was somewhat confused, at times making irrational statements. Over the thorax, upper arms, and abdomen there were well-defined, irregular, brownish, macular blotches, faded purpuric spots. There were tophi in the pinna of each ear. The heart was not enlarged. The walls of the radial arteries were palpable. Blood-pressure was 155 mm. systolic and 95 mm. diastolic. The liver edge was palpable 4 cm. below the right costal margin. The abdomen contained no fluid. The middle and ring fingers of the right hand were somewhat spindle shaped due to thickening of the periarticular tissues of the first and second phalanges. There was marked thickening about the distal joint of the left little finger. There was marked soft edema of the ankles and legs. The legs were covered with large, crimson, purpuric blotches.

The electrocardiogram showed left ventricular preponderance. Summary of radiographic findings: Localized proliferative

and slight atrophic bony changes were found. The majority of the bones and joints of the hands and feet appeared normal. Focal areas of decreased density occurred in certain of the phalanges.

**Clinical Pathology.**—*Urine.*—The numerous examinations of the urine, made during different admissions to the hospital, usually showed nothing abnormal during the interim between attacks of arthritis; during attacks a slight trace of albumin and a few casts were often present. Phthalein excretion was 24 per cent. The two-hour renal test was essentially normal; 5 per cent. of injected purin nitrogen was recovered from the urine as uric acid. After an intravenous injection of 0.5 gm. of uric acid the amount of that substance was not increased in the urine. *Blood:* Hemoglobin was 63 per cent. White cells were 9000 per c.mm. Non-protein nitrogen was 54 mgm., urea nitrogen 28 mgm., and uric acid from 3.5 to 5 mgm. per 100 c.c. of blood. Sodium urate crystals were demonstrated in a tophus in the ear.

**Progress.**—While under observation the patient developed acute gout. The attack began October 12th as swelling and pain in the metacarpophalangeal joint of the right index-finger and to a less extent in the right wrist. Within two days (October 14th) the finger joint was much swollen, somewhat reddened, hot, and tender; the wrist was similarly affected except that it was not reddened. There was constant dull aching pain in these joints and marked pain on motion. During the night time the constant pain was very severe. Within another twenty-four hours (October 15th) the right elbow and the metacarpophalangeal joints of the right index-finger and middle fingers were swollen, reddened, tender, and painful. The pain was aching in character, constant, and severe. On October 16th the affected joints were painful only on motion. By October 19th the arthritis in the right elbow had subsided. The right wrist and the two metacarpophalangeal joints remained painful on motion. All the joints of the first two fingers and the metacarpophalangeal joint of the thumb of the left hand now became swollen, reddened, tender, but were painful only on motion. On October 22d the above-described arthritis was subsiding, but

the terminal joint of the left little finger became acutely involved. By October 28th the gouty attack had subsided without medication. A feature characterizing the acute stages of arthritis was the severe aching pain in the joints when they were at complete rest. At the onset of the arthritis (October 12th) the temperature rose to 100° F., and during the attack oscillated between 100° and 102° F., reaching normal again on October 25th. During the febrile period the pulse varied between 90 and 100 per minute.

During damp weather more or less arthritic pain occurred and corresponded in character to that common in cases of chronic arthritis.

**CASE III.**—W. P. G., Med. Nos. 5471, 6625. Negro, male, restauranteur, aged forty-three. Admitted to the Peter Bent Brigham Hospital October 19, 1916, and discharged improved November 14, 1916.

**Diagnosis.**—Gout.

The patient's father suffered more or less with "chronic rheumatism," but his symptoms were unlike those of the patient. The mother died of apoplexy. Between the years 1906 and 1911 the patient worked in a paint shop. Since then he had been a restauranteur. For a number of years the appetite had been poor and mild dyspeptic symptoms frequently occurred. The patient had never taken alcoholic drinks.

**Arthritic History.**—Eighteen years ago an attack of severely painful arthritis occurred in one great toe, tarsus, and ankle. Further history of the attack was indefinite. During the next five years several similar attacks occurred. Thirteen years ago an elbow-joint was swollen and excruciatingly painful for a period of one week. Severe attacks of arthritis affecting the hands, feet, and knees have occurred every year in March or April for the past ten years. In these attacks the pain would be excruciating and the tenderness extreme. In the interim attacks of minor severity occurred at fairly frequent intervals. About six years ago the left thumb became painful and swollen. One night he thrust a needle into the swelling and expressed

white material looking like putty and soon hardening into a substance that looked "like plaster of Paris and was just as white."

**Physical Examination.**—The patient was a well-developed and nourished male negro. There were several tophi in the pinnæ of the ears. The heart was not enlarged. Its sounds were normal and there were no murmurs. The walls of the radial arteries were somewhat thickened. Blood-pressure was



Fig. 185.—This plate represents the hands of the patient reported in Case III. Tophi are shown on all the fingers except the left middle finger.

135 mm. systolic and 95 mm. diastolic. All the fingers, except the left middle finger, were deformed by numerous large tophi. Some of these involved the skin, producing white, opaque areas. The most extensive changes were seen in the thumb and forefinger of the left hand and the thumb and little finger of the right hand. In the tophi were numerous minute openings of discharging sinuses.

**Summary of the Radiographic Findings.**—Proliferative, atrophic, and destructive changes were found. Not all the

bones and joint spaces were affected. In the feet all the bones showed slight atrophy, but the proliferative and destructive changes were irregularly distributed. Many focal areas of decreased density were present. Most of these were in areas showing other bony changes. The soft tissues of the fingers showed nodular thickenings.



Fig. 186.—This is the radiogram of the hands of the patient reported in Case III. Areas of decreased bony density, appearing like bony cysts, are present in both little fingers and in the last phalanx of the right thumb. The tophus in the left little finger discharged through a sinus to the exterior. The discharge contained leukocytes and sodium urate crystals.

**Clinical Pathology.**—*Urine.*—In one of the five urine examinations the slightest possible trace of albumin was found with the heat and acetic acid test. The sediment contained no pathologic elements. Phthalein excretion was 42 per cent. The two-hour renal test showed: fixation of specific gravity; relative increase in the night amount of urine; considerable fixation of

the percentage concentration and amount of nitrogen; and some fixation of the percentage concentration and of the amount of sodium chlorid; 14 per cent. of intravenously injected uric acid was recovered in the urine.

**Blood.**—Hemoglobin was 95 per cent. White cells were 8000 per c.mm. Urea nitrogen was 30 mgm., non-protein nitrogen from 44 to 50 mgm., and uric acid 4 mgm. per 100 c.c. of blood. Wassermann reaction in the blood-serum was negative. Sodium urate crystals were demonstrated in a tophus in the ear.

Basal metabolism, determined by indirect calorimetry and calculated according to the linear formula of DuBois, was 84 per cent.

**Progress.**—During his stay in the hospital—after the first admission—on two occasions, at night, the patient complained of severe, aching pain in the right great toe joint and in an area, the size of a dime, over the internal condyle of the upper end of the tibia. The second admission was in May, 1917. In the interim between admissions five attacks of "real, good, old gout" occurred; two in the feet and three in the hands. During his stay in the hospital after the second admission the hands, especially the fingers, and the left wrist became severely painful, aching constantly, swollen, and tender. This was accompanied by a rise in temperature to 100° F. The condition was quickly relieved by the administration of wine of colchicum.

On damp days more or less joint pain occurred and corresponded in character to that common in cases of chronic arthritis. In July, 1919 the patient stated that during the last two years joint pain of severe aching nature and persisting a few hours occurred rather frequently. This pain was relieved by wine of colchicum. During this period no acute attacks of gout occurred, probably having been warded off by the use of wine of colchicum.

**CASE IV.—W. C. B.,** Med. No. 10,684. White male, physician, aged sixty-one. Admitted to the Peter Bent Brigham Hospital March 15, 1919, and discharged improved April 4, 1919.

**Diagnosis.**—Gout; chronic nephritis; hypertension.

There was no family history of arthritis or gout. The patient's habits were good. He rarely tasted alcoholic drinks.

**Arthritic History.**—The first attack of arthritis occurred about ten years ago. Since then there had been one attack a year. Up until the last attack in January, 1919, the arthritis affected either the left or the right ankle-joint, but never one and then the other, and never both at the same time. The attacks began at night. Patient awoke with a moderate, grinding pain in the ankle, which gradually became worse over a period of forty-eight hours. Within a few hours after the onset the affected joint swelled considerably. The tenderness was always moderate; the weight of the bedclothes was not uncomfortable, and palpation, if light, was not especially painful. The pain was greatly relieved by placing the affected part at complete rest, while the least motion was extremely painful. There was not much redness of the joint. Attacks lasted about one week. The last attack was in January, 1919. It began at night with some pain and tenderness of the left tendo achillis. The next morning the ankle and tarsal joints (but not the toe joints) were considerably swollen, much reddened, fairly tender, and extremely painful on motion, but not painful when at rest. This attack lasted ten days and then began to subside. General sweats did not occur. The fever reached 100° F. by mouth at a maximum (patient took his own temperature). Relief from the attacks of arthritis have always been obtained by the use of salicylates.

**Present Illness.**—This began four weeks before admission to the hospital in the right ankle, with moderately severe pain on walking and a little swelling. A few days after the onset the right knee became swollen, tender, and motion became painful enough to prevent walking. A day later the left knee-joint was similarly inflamed. At the time of admission only the right ankle and left knee remained involved.

**Physical Examination.**—Small tophi were found in the auricles of both ears. From them sodium urate crystals were obtained. The area of relative cardiac dulness measured 12.5 cm. to the left and 4 cm. to the right of the midsternal line. At

the apex a soft systolic murmur accompanied the first sound. All accessible arteries were sclerosed. Blood-pressure was 200 mm. systolic and 115 mm. diastolic. The left knee was swollen enough to cause floating of the patella. There was considerable tenderness on palpation. Motion caused moderate severe pain. The overlying skin was not changed in color, but there was local heat. The right ankle was slightly swollen, but not redened. It was less painful on motion than the left knee.

Summary of the radiographic findings: Focal areas of decreased density occurred in the heads of the first metatarsal bones.

**Clinical Pathology.**—*Urine.*—Showed a trace of albumin, a variable number of casts and leukocytes. Phthalein excretion for two hours was 5 per cent. on March 17th, a trace on March 19th, and 14 per cent. on April 2d (eighteen days after admission).

*Blood.*—Hemoglobin was 80 per cent. White cells on March 15th, the day of admission, were 13,600 per c.mm. One week later, March 21st, they were 8200 per c.mm. The urea nitrogen per 100 c.c. of blood was 74 mgm. on March 19th, 83 mgm. on March 22d, and 56 mgm. on April 2d. Uric acid per 100 c.c. of blood was 8 mgm. on March 22d. Sodium urate crystals were demonstrated in a tophus in the ear.

**Progress.**—On admission the patient was given sodium salicylate in 2-gm. doses every three hours. This promptly controlled the arthritic pain. After five days tinnitus caused the cessation of the drug, and following its omission some pain returned. The inflammatory signs in the knee and ankle gradually disappeared, and by March 28th both of these joints were again free from all acute symptoms. During the first four days in the hospital the temperature varied from 98° to 100° F. After that it was normal.

A few days after discharge from the hospital another attack of acute gout occurred. This was quickly relieved by 0.0006-gm. doses of colchicin. Since that time the patient has been able to ward off further gouty attacks by the timely use of colchicin. On May 19th non-protein nitrogen was 79 mgm. per 100 c.c. of blood. On a very restricted protein intake this had fallen to 56 mgm. on May 26th. On a more liberal protein diet the non-

protein nitrogen had risen to 71 mgm. on June 28th; the urea nitrogen was 50 mgm. and the uric acid 7 mgm. per 100 c.c. of blood. On July 8th non-protein nitrogen was 83 mgm. and uric acid 6 mgm. per 100 c.c. of blood. On September 15th non-protein nitrogen was 71 mgm., urea nitrogen 46 mgm., and uric acid 5 mgm. per 100 c.c. of blood. Since June 28th the patient had been on a restricted protein intake, but without effect on the blood findings.

**CASE V.**—F. J. S., Med. No. 6154. White male, druggist, aged forty-three. Admitted to the Peter Bent Brigham Hospital February 16, 1917, and discharged improved March 8, 1917.

**Diagnosis.**—Gout; obesity.

The father had died of heart disease at sixty-seven years, the mother of erysipelas at fifty-five years. One sister had apoplexy at fifty-seven years. Prior to five years ago the patient consumed 3 to 4 glasses of whisky daily. The patient had undergone an operation for umbilical hernia in 1916. For the past seven years there had been some burning on urinating, and for the past seven months there had been nocturia once or twice at night. The present weight was 250 pounds.

**Arthritic History.**—The first attack of arthritis occurred in December, 1906. Late one evening the left knee became painful on walking, but during the night the patient's sleep was not disturbed. The patient sat up in a chair and directed his business the next day. By the evening of this day the left knee was greatly swollen, too tender to bear the slightest touch (not even the weight of bedclothes), fiery red in color, but painful only on motion. There were no sweats or feverishness, but the patient remembered that the thermometer showed some pyrexia. The acute symptoms persisted for six weeks, remaining localized to the knee-joint. Then during the next twelve weeks the swelling and tenderness and then the pain on motion subsided. The next attack occurred in 1907. From 1907 to 1913, inclusive, attacks occurred once or twice each year and affected the knees, ankles, and metatarsophalangeal joints of the halluces. Some attacks were monarticular and others polyarticular, beginning in

one joint, partially subsiding within a few days, and then affecting the other joints mentioned. The presence of fever and sweats and other details of these attacks were not remembered. Since 1914 two prodromal symptoms have preceded the attacks: (1) A persistent and constant burning sensation in the glans penis for a week previous to the onset of an arthritis; and (2) stiffness of the joint or joints, which were to be affected, for two or three days before the onset. The onset was characterized by pain in the affected joints on motion, and within a few hours this increased to such an extent that walking was impossible and the slightest motion was excruciatingly painful. But there was no pain when the joints were kept completely quiet. Great swelling and extreme tenderness were constant symptoms, but redness was not marked. Since 1914 all attacks but one have been polyarticular, beginning with equal frequency in the knees, ankles, or one of the metatarsophalangeal joints of any one of the toes, and later involving one or more of the joints enumerated. There were no sweats. The temperature ranged between 101° and 102° F. In the summer of 1916 an attack occurred which affected only the first phalangeal joint of the middle finger of the right hand. Its duration was four days.

The present attack of arthritis began nine days (February 7, 1917) before admission to the hospital. The prodromes above mentioned were present, the right ankle being stiff for three days previous to the onset. This joint then became painful on motion, but the patient was able to hobble around during the first day. On the next day all the signs above mentioned as characterizing the acute arthritis were present. The second day after the onset the left knee-joint became somewhat painful on motion, but no other signs of inflammation developed. In 1911 a traveling man told the patient that his attacks were due to gout and recommended colchicin. This drug has always given the patient relief, while salicylates have never done so.

**Physical Examination.**—The patient was a well-developed, obese man. The right ear contained a small tophus. The heart measured 12 cm. to the left and 3 cm. to the right of the mid-sternal line. The sounds were normal and there were no mur-

murs. The radial arteries were not sclerosed. Blood-pressure was 130 mm. systolic and 90 mm. diastolic. The left knee was slightly larger than the right and motion caused great pain. The right ankle was somewhat swollen and flexion caused considerable pain.

The electrocardiogram showed left ventricular preponderance.

Summary of radiographic findings: Slight proliferative changes affected the bones of the first metatarsophalangeal joints. A focal area of decreased density was found in the head of the left first metatarsal bone.

**Clinical Pathology.**—*Urine.*—On one of three examinations the urine contained the slightest possible trace of albumin with the heat and acetic acid test. The sediment contained no pathologic elements. Phthalein excretion was 50 per cent. on February 17th and 21 per cent. on March 1st. The two-hour renal test showed some increase of the night amount of urine (660 c.c.).

*Blood.*—Hemoglobin was 90 per cent. White cells were 10,000 per c.mm. The red cells and the differential count were normal. Urea nitrogen was 26 mgm., non-protein nitrogen 44 mgm., and uric acid 5 mgm. per 100 c.c. of blood. Sodium urate crystals were demonstrated in a tophus in the ear.

Basal metabolism, determined by indirect calorimetry and calculated according to the linear formula of DuBois, was 83 per cent.

**Progress.**—The acute stage of the arthritis persisted for three weeks from the date of onset. On admission the temperature was 101.5° F. and the pulse 80 per minute. Both of these returned to normal and the arthritis subsided after the administration of colchicum for four days. However, the left knee at this time remained a little stiff and slightly painful on motion.

**CASE VI.**—G. W. L., Med. Nos. 236, 2929. White male, special police officer, aged sixty-eight. Admitted to the Peter Bent Brigham Hospital July 22, 1913, and discharged improved August 16, 1913.

**Diagnosis.**—Gout (acute and chronic); arteriosclerosis; vascular hypertension.

The patient's mother had had arthritis resembling his own. The patient had been a moderate beer drinker. Several months before admission to the hospital, in 1913, a urinary calculus had been passed in the urine.

**Arthritic History.**—This began in 1903. There was first noticed tenderness in the fourth toe of the left foot. This tenderness gradually increased, the toe became greatly swollen, and by the end of six months from the onset of symptoms walking was rendered very painful. At about this time the great toe of the right foot became ulcerated and was finally amputated. During the past eight years tophi had developed about the second and third joints of all the fingers except the middle finger and thumb of the right hand. Beginning as tender nodules, the tophi had increased in size up to the present time. In 1913 the patient first noticed tophi in the ears and a "lump" (a tophus) on the right elbow. Twice in the six months prior to the last admission he experienced a sensation in the right knee, in an area of about the size of a dollar, as if he had been struck with a hammer. There had been, however, no "rheumatic" pain.

**Present Illness.**—The patient entered the hospital for the purpose of having a large tophus removed from the right heel.

**Physical Examination.**—Two small, nodular tophi were present in the pinna of the right ear and one in the left. From them sodium urate crystals were obtained. The heart was not enlarged. The walls of the radial arteries were thickened and tortuous. Blood-pressure was 160 mm. systolic, 95 mm. (1913) and 120 mm. (1915) diastolic. Over the olecranon process of the right ulna there was a rather firm, non-tender, nodular swelling (tophus) about the size of the end of a man's thumb. The skin over this nodule was freely movable. The terminal phalanx of the third finger of the right hand was missing. All the remaining fingers of this hand and those of the left hand, except the middle finger, showed nodular enlargements (tophi) about the phalangeal joints. The articular ends of the bones of the

phalanges were enlarged. The toes were moderately deformed, probably due to improperly fitting shoes. The metatarsal joints were somewhat enlarged. Protruding posteriorly from the right heel was a non-tender, resilient nodule (tophus), measuring 2.5 x 1.5 x 1.5 cm., in the center of which was a small ulcerated area.

**Summary of the Radiographic Findings.**—The bones of both hands and feet showed hypertrophic changes at the margins of the phalangeal joints and of the metacarpo- and metatarsophalangeal joints. Along the shafts of the phalanges were exostoses, the so-called Bruce's nodes. In the region of the interphalangeal joints, principally the second, and of the first metatarsophalangeal joints the margins of the bones showed semi-circular, punched-out areas of decreased density.

**Clinical Pathology.**—*Urine.*—On the first admission, in 1913, a trace of albumin was noted in four examinations of the urine. In 1915 the very slightest trace was found in three examinations. In one examination in 1915 a number of hyaline casts were present, but in other examinations, in 1915 and 1913, either none or a very scanty number were found. Phthalein excretion in two hours was 80 per cent. in 1913 and 60 per cent. in 1915.

*Blood.*—Hemoglobin was 90 per cent. and white cells 8000 per c.mm. Smears were normal. The Wassermann reaction in the serum was negative. In 1915 blood uric acid was 5 mgm. per 100 c.c. on two examinations and urea nitrogen 19 mgm. per 100 c.c.

**Progress.**—During both admissions, 1913 and 1915, acute gouty attacks occurred. In 1913 the attack began in the right hand and fingers and the right wrist. It was characterized by marked and constant pain, great swelling and heat of the affected parts. The entire hand, especially the little finger, was deeply reddened. With aspirin, colchicum, and atophan the arthritis subsided within four days. There was a mild febrile reaction, 100° F. A few days later both great toes became similarly affected. This attack subsided within a few days. In 1915 the attack began with pain in the third finger of the left hand and in the left wrist. The finger was swollen, cherry red in color, hot to the touch, and exquisitely tender. The wrist

was swollen and hot, but not reddened. The attack was accompanied by a rise of temperature to 100° F. Four days later the left foot and ankle became edematous, slightly reddened, and fairly tender. Nine days after the onset of this attack the left hand and wrist had returned to normal, the left ankle and foot retained some swelling, and mild pain began in the left elbow. Within two weeks the attack had entirely subsided following the use of atophan.

**CASE VII.**—P. S. D., Med. No. 5889. White male, freight clerk, aged fifty-eight. Admitted to the Peter Bent Brigham Hospital January 4, 1917, and discharged improved January 20, 1917.

**Diagnosis.**—Gout; chronic nephritis; arteriosclerosis; gastric ulcer (perforated); secondary anemia.

The family history was essentially negative. The patient's habits were good. He did not use alcoholic beverages. He was admitted to the hospital because of symptoms due to gastric ulcer.

**Arthritic History.**—Twelve years ago the left great toe joint became very painful about midnight. The joint was exquisitely painful even at rest, and by morning was very red and swollen. A doctor was called, who said that the trouble was due to an old injury, and advised hot poultices. These were tried, with the result "that it nearly drove me wild." The joint was very much worse at night, but during the day he was able to get about the house without very much pain. After a couple of weeks he changed to another doctor, who applied ichthyl to the joint, and the pain left within a few hours. The use of ichthyl kept the pain more or less controlled. After five weeks the attack was over and he was able to go back to work. Ten years ago a second attack began about midnight, similar in character to the previous attack. It began first in the left toe joint and on the next day the right great toe also became affected, then in a few days the ankle, heel, and instep of both feet became involved. The pain would jump about from place to place every day or two; and after three weeks the attack subsided. In this attack ichthyl was used without effect on the condition. Six

years ago a third attack came on which was essentially like the first two, and in two days both great toe joints, both ankles, and the wrist, knuckles, and fingers of the left hand became involved and were intensely painful, swollen, and reddened. During this attack the patient says "he hated to see night coming on because of the increased pain in the joints." This attack kept him about the house or in bed for three to four weeks, and then he went to work, but still had more or less trouble at night for three months. Five years ago the next attack came on and involved the hands, feet, and ankles, but was not severe enough to keep him from work. Three years ago he had the worst attack he had ever had. This one involved both hands, fingers, wrists, ankles, feet and toes, and kept him in bed for one month. During this time he was so crippled up that he could not feed himself. After getting out of bed he was about the house five weeks before going to work again. About this time he first noticed small nodules in his ears, which he thought were "black-heads." These nodules were painful at times, but usually caused no discomfort. Two years ago and again one year ago he had slight attacks of arthritis of a very mild nature, which occurred in the winter, did not keep him from work, and lasted but a few days. One year ago he had the last attack, which was fairly severe and kept him from work two weeks. The toes, ankles, and hands were involved in this attack. Changes in the shape of the great toe joints have been present since about twelve years ago and began following the wearing of a tight pair of shoes.

**Physical Examination.**—The patient showed signs of secondary anemia due to hemorrhages from the gastric ulcer. Many small tophi from which sodium urate crystals were obtained were present in the auricles of both ears. The heart was not enlarged. The radial arteries were sclerosed. Blood-pressure was 138 mm. systolic and 70 mm. diastolic. The spine in the dorsal region was rigid and showed a marked kyphosis. The small joints of the fingers and the great toe joints showed evidence of the changes of chronic arthritis.

**Summary of Radiographic Findings.**—The bones of both ankle-joints and tarsi showed bone atrophy, which was more

marked in the left foot. There was spur formation at the insertions of both tendo achilles, more marked on the left. Proliferative changes in the bones of the left ankle-joint and tarsus were present.

**Clinical Pathology.**—*Urine*.—Examinations showed a slight trace of albumin and a few hyaline casts. Phthalein excretion was 12 per cent. in two hours.

*Blood*.—Hemoglobin was 35 per cent. There were 2,208,000 red cells and 4611 white cells per c.mm. The blood contained 3.3 mgm. of uric acid and 62 mgm. of non-protein nitrogen per 100 c.c. Sodium urate crystals were demonstrated in a tophus in the ear.

**CASE VIII.**—A. S., Med. No. 10,638. White, female, box factory worker, aged thirty-nine. Admitted to the Peter Bent Brigham Hospital March 6, 1919, and discharged improved May 1, 1919.

**Diagnosis.**—Gout; chronic nephritis; hypertension; syphilitic aortitis; aortic insufficiency; retroflexion of uterus; menorrhagia.

The patient's father died of cancer of the stomach. There was no family history of gout or "rheumatism." The patient had been a moderate user of alcoholic drinks. Three months before admission to the hospital she had had mild "rheumatism" of the right shoulder-joint. For the past six years she had had occasional attacks of mild dyspepsia. She entered the hospital because of dyspnea on exertion, anorexia with occasional vomiting, and dull pain over the sternum and in the right shoulder, and a severe leukorrhea.

**Arthritic History.**—First attack of arthritis occurred in the winter of 1914 (five years ago), and a second one in the winter of 1918. In the interim between these attacks, which were severe, there occurred transient milder attacks of arthritis. Attack of 1914: Arthritis began on Sunday afternoon in both ankles and feet. They were greatly swollen, reddened, exquisitely tender (weight of sheet could not be borne), and extraordinarily painful. Within a few days the feet were described

as becoming very dark in color. This attack lasted two weeks and then began to subside. The attack in 1917 resembled the first attack. It persisted for four weeks. Attack of 1918: Arthritis was in both ankles and feet and in the left wrist, metacarpals, and metacarpophalangeal joints. It persisted for two weeks. Since 1914 there had been attacks of arthritis of a few days' duration which occurred a few times a year, irrespective of the season. These attacks began without known cause and usually as a podagra. At times the ankles were also involved. The affected joint became much reddened, slightly swollen, there was sharp shooting pain, and exquisite tenderness (weight of bed sheet could not be borne). The joints were extremely painful even when at complete rest.

**Physical Examination.**—Small tophi, from which sodium urate crystals were obtained, were present in the auricles of the ears. The area of relative cardiac dulness measured 13.5 cm. to the left of the midsternal line. A blowing, diastolic murmur was heard all over the sternum, with the point of maximum intensity at the junction of the sternum and the fourth costal cartilage. No peripheral signs of aortic insufficiency were found. The radial arterial wall was thickened, but not beaded. Blood-pressure was 218 mm. systolic and 134 diastolic. The metatarsophalangeal joints of both great toes were moderately enlarged.

**Electrocardiogram.**—There was left ventricular preponderance and the *P* waves were inverted in Lead III.

**Summary of Radiographic Findings.**—There were focal areas of decreased density in the heads of the first metatarsal bones.

**Clinical Pathology.**—*Urine.*—Eight urine examinations were made. From a small trace to a trace of albumin was found. The sediment contained a considerable number of leukocytes and rarely a hyaline or cellular cast. Phthalein excretion on March 10th was 35 per cent., on April 9th, 25 per cent., and on April 22d, 35 per cent. The two-hour renal test showed nocturnal diuresis (770 c.c.) and low salt excretion (1.78 gm.).

**Blood.**—Hemoglobin was 80 per cent. The white cells varied from 7000 to 12,000 per c.m.m. The red blood-cells and the

differential count of leukocytes were normal. The blood urea nitrogen varied from 26 to 34 mgm. per 100 c.c. Non-protein nitrogen was 35 to 46 mgm. per 100 c.c. of blood. The uric acid content of the blood varied from 6 to 8 mgm. per 100 c.c.

Cerebrospinal fluid showed 6 cells per cubic millimeter and no globulin.

The Wassermann reaction in the blood-serum was strongly positive, and in 2 c.c. of cerebrospinal fluid was negative. Sodium urate crystals were demonstrated in a tophus in the ear.

**Progress.**—During the first week in April the patient had a short attack of podagra, unaccompanied with fever. From April 15th to 26th menorrhagia occurred. The patient improved symptomatically, and April 10th was free from subjective symptoms.

**CASE IX.**—M. W. S., Med. No. 6264. White male, salesman, aged forty. Admitted to the Peter Bent Brigham Hospital March 10, 1917, and discharged improved April 25, 1917.

**Diagnosis.**—Gout; chronic nephritis; hypertension; uremia (acute); tumor in left testicle; congenital heart lesion; (?) of patent ductus arteriosus.

The patient's father died of pneumonia and the mother of carcinoma of the uterus. The patient entered the hospital in a semicomatoso condition due to acute uremia. He had used "considerable" alcoholic drinks for years. He was a salesman. During the past five months he had had edema of the feet and ankles during the day and disappearing at night. Sixteen years ago he was refused life insurance because of "kidney trouble." Several years ago he sustained trauma to the right testicle, which began to enlarge three years ago, and lately has increased in size rapidly.

**Arthritic History.**—First attack occurred twenty-five years ago (at the age of sixteen) in the first phalangeal joint of the index-finger of the right hand. The attack began during the day; the onset was sudden, with very severe aching and continuous pain, great swelling of the joint, extreme tenderness, and scarlet red in color. Pain prevented sleeping. Duration of acute stage

was five days, and then the inflammation gradually subsided. Patient states attack was accompanied with much fever, but sweating not remembered. Second attack occurred the following year. It was in the same joint and of the same character as the first attack. Since the first attack patient has had one to two each year up to the present time. Each attack has been characterized by extreme, constant pain, even at complete rest, great swelling of the affected joints, deep scarlet redness of the overlying skin, and since the attacks became polyarticular there have been heavy sweats and always much fever. The pain has been worse usually at night. The onset has been either during the day or during the night. The onset was with some pain on motion in the joint or joints which would be affected, and then within a few hours the inflammation was at its height. For the last twenty years the attacks had been polyarticular, affecting the elbows, the wrists, the first phalangeal joints of the left index-finger, the knees, the ankles, the metatarsophalangeal joints of both halluces, and the first phalangeal joints of both halluces. Attacks had been confined to the lower extremities or to the upper extremities, but had never occurred in both at the same time. The arthritis began in some one of these joints (no more frequently in one than in the other), and without subsiding in this joint others became severely affected after a few days. Polyarticular attacks lasted from one to seven weeks.

**Present Illness.**—The last attack began March 8, 1917, in the right wrist, and was of its usual severity, however, by March 11, 1917. On the morning of March 9, 1917, patient suddenly became unconscious, his face became deeply reddened, his breathing stertorous, and for about half an hour there was clonic spasm of both arms. At the end of this time the patient became conscious and all symptoms disappeared. There was no memory of what had occurred by the patient. His vision was blurred and patient was confused following the comatose condition. Within an hour a second coma came on. In this the face reddened and the breathing became stertorous, as during the first attack. There were no spasms, but the patient bit his tongue and thrashed about so that he had to be held in bed. Recovery from coma

occurred about midnight of March 10, 1917, in the Peter Bent Brigham Hospital. Patient was confused, with poor memory until March 12, 1917. Since then patient has remained in as good physical and mental condition as previous to his present illness.

**Physical Examination.**—The patient was a well-nourished man lying in a stuporous condition. A small tophus was present in each ear from which sodium urate crystals were obtained. The area of cardiac dulness measured 13 cm. to the left in the fifth interspace, and 4 cm. to the right in the fourth interspace. A loud, rough systolic murmur was audible over the precordium, and of maximum intensity along the left sternal margin and in the pulmonic area. The heart's action was regular. The walls of the radial arteries were barely palpable. Blood-pressure was 200 mm. systolic and 100 mm. diastolic. There was some swelling of the right hand and wrist.

**Clinical Pathology.**—*Urine.*—Examinations of the urine from March 11th to April 10th showed a specific gravity varying from 1.004 to 1.022, a heavy trace of albumin, numerous casts, and a variable number of leukocytes, erythrocytes, and epithelial cells. The specimens examined subsequently and up to April 25th contained less albumin. Phthalein excretion for two hours was 21 per cent. on March 20th, 40 per cent. on April 4th, and 30 per cent. on April 16th.

**Blood.**—Hemoglobin was 95 per cent. and white cells 24,600 per c.m.m. on March 10th. White cells were 12,600 on March 12th. Urea nitrogen per 100 c.c. of blood was 27 mgm. on March 10th, 49 mgm. on March 12th, 31 mgm. on March 27th, 27 mgm. on April 4th, and 29 mgm. on April 18th. Non-protein nitrogen was 45 mgm. on March 25th. On March 10th blood  $\text{CO}_2$  was 31 per cent. Sodium urate crystals were demonstrated in a tophus in the ear.

Basal metabolism, determined by indirect calorimetry and calculated according to the linear formula of DuBois, was 88 per cent.

**Progress.**—Within two weeks and a half after admission to the hospital (March 27th) the patient had recovered from the

attack of uremia and gout. On a purin-free diet the amount of blood-urea nitrogen had fallen considerably and the phthalein excretion had increased.

**CASE X.—P. A., Med. No. 10,814.** White male, laborer, aged forty-nine. Admitted to the Peter Bent Brigham Hospital April 4, 1919, and discharged recovered April 9, 1919.

**Diagnosis.—Gout.**

There was no history of gout or arthritis in the family. The patient drank about 3 gallons of wine a week.

**Arthritic History.**—For the past seventeen or eighteen years attacks of arthritis in the metatarsophalangeal joint of the right great toe had occurred. These attacks recurred once a year up to thirteen years ago. Since then there had been two attacks a year. The last two attacks had started in the right hallux, and within a few days the metatarsophalangeal joint of the left great toe had also been involved. The attacks of arthritis were characterized by sudden onset, much redness, with some swelling of the affected joint, exquisite pain, and "tenderness beyond description." The pain was persistent and constant even when at complete rest in bed. Attacks occurred without relation to season and the onset at any time of day or night. (Since 1914 three attacks of iritis had occurred. Four months ago the left eye was involved.) The last attack began thirteen days before admission to the hospital. The metatarsophalangeal joint of the right great toe became swollen, red, exquisitely tender, and violently painful. The pain was knife-like in character. During the next three days the tarsus of the right, then also of the left, foot, and of the left great toe joint became similarly involved. On the fourth day the left knee became slightly swollen, and moderately tender and painful. Iritis of the right eye had been present for two weeks. Attack had practically subsided at time of admission to the hospital.

**Physical Examination.**—Two small tophi were found in the auricle of the right ear. Sodium urate crystals were obtained from them. The scleræ of the right eye was markedly injected. The heart was not enlarged. The radial arteries were not scl-

rosed. Blood-pressure was 138 systolic and 86 diastolic. There was some periarticular swelling and redness about the metatarsophalangeal joint of the right great toe. The dorsæ of both feet were slightly reddened. Neither the toes nor the feet were tender or painful.

**Summary of Radiographic Findings.**—There were slight proliferative changes and focal areas of decreased density in the head of the first metatarsal bone of the right foot.

**Clinical Pathology.**—The *urine* contained a slight trace of albumin by the heat and acetic acid test. A variable number of hyaline, granular, and cellular casts were found on different examinations. Phthalein excretion was 38 per cent. in two hours. The "two-hour renal test" was essentially negative.

**Blood.**—Hemoglobin was 75 per cent. On April 2d the non-protein nitrogen was 55 mgm. per 100 c.c. of blood, while on April 6th it had dropped to 42 mgm. On April 6th there were 6 mgm. of uric acid per 100 c.c. of blood. Sodium urate crystals were demonstrated in a tophus in the ear.

**CASE XI.**—F. C. H. S., Med. No. 1083. White male, painter, aged fifty-nine. Admitted to the Peter Bent Brigham Hospital April 16, 1914, and discharged improved April 25, 1914.

**Diagnosis.**—Gout; chronic myocarditis; auricular fibrillation.

There was no history of gout or arthritis in the family. The patient drank a gallon of whisky a month and a moderate quantity of beer. He was a painter by occupation.

**Arthritic History.**—In 1906 he had an attack of arthritis in the metatarsophalangeal joint of the right great toe. It was characterized by swelling, tenderness, and pain enough to prevent sleeping. The attack was three weeks in subsiding. In 1912 a similar attack occurred, and again in February, 1914. The latter attack persisted for three weeks.

**Present Illness.**—The patient entered the hospital because of "nervousness, dizziness, cardiac palpitation, and much dyspnea on exertion."

**Physical Examination.**—A small tophus was found in the auricle of the right ear. The area of relative cardiac dulness

measured 14 cm. to the left and 4 cm. to the right of the mid-sternal line. There were no murmurs. The heart's action was absolutely irregular. An electrocardiogram showed auricular fibrillation. Blood-pressure was 192 mm. systolic and 120 mm. diastolic. The lower border of the liver extended 6 cm. below the right costal margin. Its surface was smooth and the edge firm. The temperature reached a maximum of 100° F. the first three days in the hospital. It then fell to normal.

**Clinical Pathology.**—*Urine.*—The urine examinations were normal except for a few hyaline and granular casts found in one specimen, and an occasional red blood-cell in another. Phthalein excretion was 61 per cent. in two hours.

*Blood.*—Hemoglobin was 98 per cent. The white cells were 6000 per c.mm. In 100 c.c. of blood 6.8 mgm. of uric acid were found. Wassermann reaction in the blood-serum was negative. Sodium urate crystals were demonstrated in a tophus in the ear.

**Progress.**—On admission the metatarsophalangeal joint of the right great toe was bright red in color, hot, and tender on palpation. Motion caused considerable pain. Four days later (April 18th) the patient complained of pain in the affected joint. It was still red, tender, and slightly swollen. He was given 1.5 gm. atrophan a day, and within three days (April 21st) the attack had completely subsided.

**CASE XII.**—J. K., Med. No. 232. White male, teamster, aged forty-eight. Admitted to the Peter Bent Brigham Hospital July 21, 1913, and discharged improved July 28, 1913.

**Diagnosis.**—Gout (acute and chronic).

There was no family history of gout, renal or cardiovascular diseases. The patient for many years had drunk 2 or 3 whiskies and 2 to 3 beers a day.

**Arthritic History.**—The first attack of arthritis occurred in 1905. The metatarsophalangeal joint of the left toe was affected. It was swollen, reddened, and very painful. The acute stage lasted two days. Since then he had had other attacks, in some of which the ankles had been involved. For the previous

two years he had been free from attacks up until the spring of 1913. In this attack both feet were affected. The attacks were accompanied by malaise and anorexia. The attack present on entering the hospital began four weeks before admission. Both feet were involved. The onset was sudden. The feet became greatly swollen, deeply reddened, and the pain so acute he "could not cry." The extreme severity had subsided on admission. All attacks had occurred during the warmer months of the year.

**Physical Examination.**—Tophi were found in the auricles of both ears. The feet were much swollen, reddened, very tender, and painful on passive motion. Otherwise the physical examination was essentially negative. The cardiovascular system was normal. Blood-pressure was 132 mm. systolic and 90 mm. diastolic.

**Clinical Pathology.**—*Urine.*—There were no abnormal findings in the urine.

*Blood.*—Hemoglobin was 93 per cent. White cells were 5000 per c.mm. Wassermann reaction on the blood-serum was negative. Sodium urate crystals were demonstrated in a tophus in the ear.

**Progress.**—No fever was present. By July 25th the redness had disappeared from the feet. There was no pain if the patient kept quiet in bed. By July 28th the arthritis in the feet had disappeared. The patient was able to walk without discomfort. The treatment consisted of 1.5 gm. of atophan per day and a purin-free diet.

**CASE XIII.**—J. J. H., Med. Nos. 10,727, 10,966. White male, painter, aged thirty-nine. Admitted to the Peter Bent Brigham Hospital March 24, 1919, and discharged recovered April 15, 1919.

**Diagnosis.**—Gout.

The family history was negative for gout and the past medical history non-essential.

**Arthritic History.**—Up to two years ago the patient had drunk much beer. Since then his habits had been good. His

occupation was that of a house-painter. Seven years ago he sustained a fracture of the skull which had left the patient in a somewhat dull mental condition. Six years ago he was admitted to the Surgical Service of the Peter Bent Brigham Hospital because of arthritis of the left foot. The record taken at that time showed the patient had had an attack of arthritis of nine weeks' duration. The entire left foot and ankle were affected. On admission the left foot was slightly swollen and cyanotic. There was much swelling, discoloration, and tenderness of the left first metatarsophalangeal joint. A bunion was present on the head of the metatarsal bone of this joint. This and calluses on the balls of the feet were accredited with causing the arthritis and the pain. A resection of the head of the bone was made. Since the resection, up to the time of the present illness, the left great toe had been continually somewhat tender and stiff. In spite of his exposure to lead he had had no symptoms of poisoning.

**Present Illness.**—Began seven days prior to admission, with stiffness of the right knee. The joint did not swell and the symptoms subsided in a few days. Two days later the left knee became "red, swollen, and sore as a boil." Since then up to the date of admission to the hospital the knee had grown worse. The right first great toe joint also became painful on motion and tender. The pain in the knee and toe had not been severe when the parts were at rest, but walking had been quite painful.

The patient was able to walk to the hospital, a distance of about three blocks, without aid.

**Physical Examination.**—The physical examination showed some sclerosis of the radial arterial wall. The blood-pressure was 140 mm. systolic and 70 mm. diastolic. The heart was not enlarged. A tophus, from which sodium urate crystals were obtained, was found in the auricle of the right ear. The left knee was considerably swollen, contained fluid, was moderately tender, and fairly painful on motion. The right first metatarsophalangeal joint was slightly swollen, very tender, and moderately painful on motion.

**Summary of Radiographic Findings.**—Right foot: in a

lateral view, the head of the first metatarsal bone was mottled as the results of focal areas of decreased bony density.

**Clinical Pathology.**—*Urine.*—Six urine examinations showed no albumin, sugar, or pathologic formed elements. Phthalein excretion for two hours was 39 per cent. on March 25th and 30 per cent. on March 31st. The "two-hour renal test" showed a slightly high night amount of urine (718 c.c.) and a tendency toward hyperpermeability in the 7 to 9 A. M. specimen.

*Blood.*—Hemoglobin was 80 per cent. White cells varied from 6400 to 8800 per c.mm. Uric acid was 4 mgm. per 100 c.c. of blood on March 24th and 6 mgm. on April 7th. The non-protein nitrogen was 40 mgm. on March 24th and 36 mgm. on April 7th. Sodium urate crystals were demonstrated in a tophus in the ear.

Wassermann reaction on the blood-serum was negative.

**Progress.**—By April 1st the swelling of the knee had almost disappeared and the right great toe joint appeared normal, but was slightly tender on palpation. On April 2d the patient was given a "standard nephritic diet" and coincidentally with this there occurred increased swelling of the right knee. The joint ached moderately severely, constantly, and even when at rest. Under the use of 0.0005-gram doses of colchicin the pain ceased. By April 8th the knee had become normal again. On admission the temperature was 100° F., but dropped to normal within twenty-four hours. A rise to between 99° and 99.5° F. accompanied the second attack of arthritis on April 3d to 7th. On April 28th the patient was readmitted to the hospital. Since the previous discharge he had not been able to work. Two days prior to the last admission he had had sharp pain in the right instep on walking. On the morning of admission he awoke to find the right foot somewhat swollen and extremely painful. On physical examination there was slight swelling and redness of the skin just below the inner and outer malleoli of the right ankle. These areas were markedly tender, and passive motion of the foot caused pain in the ankle. The temperature was elevated, 99° to 100° F. After four days of the administration of colchicin all symptoms had disappeared. On May 13th

dull, aching pain and tenderness developed in the region of the left external malleolus. The temperature rose to 100° F. After the administration of atophan for two days these symptoms disappeared.

#### GENERAL SUMMARY

**Etiology.**—A family history of probable gout was present in one case (VI) and of mild chronic "rheumatism" in a second case (III). The history of considerable use of alcoholic drinks was given in all but 3 cases (III, IV, and VII). Exposure to lead was present in 2 cases (XII and XIII). All the patients were men except one. The age of onset was sixteen years in 1 case, twenty-five years in 1, thirty-one to thirty-four years in 5, forty to forty-six years in 3, and fifty-one to fifty-eight in 3.

In this series the age incidence accorded with that which is generally found, that is, in the great majority gout manifested itself not earlier than the third decade. As is usually the case, the patients were mostly men—all but one in this series. All were whites except one negro. Heredity played no rôle, except possibly in one case (VI). Both alcohol and lead are universally considered of etiologic importance. The high incidence of the use of alcohol in this series of cases supports the view that it is an etiologic factor. No symptoms of plumbism had developed in the 2 cases giving a history of exposure to lead.

**Gouty Arthritis.**—The initial attack of gouty arthritis was confined to the metatarsophalangeal joint of the great toes in 5 cases (VII, X, XI, XII, and XIII). The arthritis was polyarticular in 8 of the cases. In 3 of these the onset occurred in one joint and quickly spread to others. In 5 cases the arthritis was polyarticular from the start. The joints first affected in the initial attack in each case were: both hip-joints (Case I); the wrist and fingers (Case II); the great toe joint (Case III); both ankle-joints (Case IV); both knees (Case V); the metatarsophalangeal joint of the fourth toe (Case VI); the ankles and tarsi (Case VIII); and the metacarpophalangeal joint of the index-finger (Case IX).

In 12 of the 13 cases attacks of polyarticular arthritis de-

veloped; in fact, the arthritis became more often poly- than mono-articular. In these attacks the metatarsophalangeal joint of the great toe was not always affected. The joints involved in polyarticular attacks were: the great toe joints, 12 cases; the ankle-joints, 11 cases; the tarsal joints, 10 cases; the knee-joints, 8 cases; the phalangeal joints, 8 cases; the wrist-joints, 7 cases; the metacarpophalangeal joints, 4 cases; shoulder-joints, 2 cases; and the toe joints (other than the great toes), 2 cases. Every joint in the body, including the temporomandibular and the intervertebral, had been affected in different attacks of arthritis in Case I. In 1 case (XI) the arthritic attacks remained confined to the great toe joint. In another case (IV) the great toe joint had never been affected.

The onset of the arthritis was sudden, and the symptoms had reached their acme within a few hours in 9 of the cases (I, III, IV, VI-X, and XII). In 2 cases the acme was not reached until one to two days had elapsed (Cases II and V). The duration and severity of the attacks were variable, both in the same case and among the different cases. Severely painful attacks were common to all. In such attacks the acute stages persisted from a few days (Cases VI and XII) to from five to ten weeks (Cases I, V, IX, XII). After the acute stages had subsided complete recovery occurred in from a few days to a week. In several cases milder attacks of arthritis occurred in the interim between severe ones. Frequent joint aching or repeated arthritic attacks made life very uncomfortable for certain cases (see Cases I and III).

In certain cases, *e. g.*, I, II, and V, the arthritis would largely subside in one joint, only to appear simultaneously in another. In this respect it resembled the arthritis of acute rheumatic fever.

The acute attacks of arthritis were frequently accompanied by febrile reaction. This was usually slight, but occasionally reached 102° or 103° F. The number of white blood-cells either remained normal or a mild leukocytosis occurred.

Definite figures cannot be given for the number of recurrences of the gouty arthritis. It may be stated with accuracy

that attacks varied, among the different cases, from a few up to probably twenty (Case I).

The severer attacks of arthritis which occurred in the cases of this series may be divided into two classes (depending on the character of the pain), as follows:

1. In the first class the joints were swollen, intensely redened, exquisitely tender, and excruciatingly painful even when at complete rest (see Cases I-III, VI-XIII). The appearance and symptoms often resembled an acute, suppurative arthritis. The most marked feature was the severity and constancy of the pain. Patients with this type of gout often became so accustomed to pain that in narrating their medical histories they forgot to mention that feature of their disease. This type is the so-called *acute regular gout*.

2. The second and less common class differs from the first largely in the character of the pain. In this class pain is present only on motion of the affected joint (Cases IV and V).

The arthritis may, also, be divided into a mono-articular type (Case XI) and a polyarticular type. In certain cases chronic arthritis was a marked feature (Cases I-III).

The literature on gout commonly states that arthritis involving the metatarsophalangeal joint of the great toe is a most characteristic feature of gout. In practical clinical diagnosis it has become the custom to consider gout whenever an arthritis of that joint occurs. A study of the cases of this series justifies that custom. However, in the cases of this series gout affected other joints almost as frequently as it did that of the great toe. In one case (IV) the latter had never been involved, and it was not always affected in the attacks of the other cases; as, for example, in an attack occurring while Case II was under observation. For this reason gout should always be considered as a possible cause of every case of arthritis.

**Tophi** were present in the pinnae of the ears in every case of this series. They were also present on the fingers in 3 cases (Plate I) and about the elbow-joints in 1 case.

**Renal Function.**—In 6 cases of this series in which the clinical diagnosis of nephritis was not justifiable renal function was

studied. The tests employed were phthalein excretion, the urea and non-protein nitrogen content of the blood, and the "two-hour renal test." By means of these tests some disturbance in renal function was demonstrated in each case. This demonstration of disturbed renal function in non-nephritic gouty cases raises the question as to whether the reputed disturbances in metabolism of the purins, especially uric acid, in gout occur. Of these disturbances only one has been proved; that is, the deposition of sodium urate in the tissues (tophi). All other contentions that metabolic disturbances occur in gout are based: (1) upon the phenomena of diminished excretion into the urine of purin bodies, especially uric acid; and (2) to a lesser extent upon the high uric acid content of the blood. These phenomena may be adequately explained as the result of uric acid and purin-nitrogen retention by the kidneys. The most direct, although not conclusive, evidence that the kidneys retain uric acid has been shown by the experiments of the author<sup>1</sup> and co-workers. In one set of experiments retention of uric acid in gout and in non-gouty nephritis was demonstrated after the intravenous injection of that substance. Further evidence against disturbances in purin metabolism was the failure to demonstrate abnormalities in heat production, as shown by indirect calorimetry, after the feeding of foods rich in nucleins. If disturbed renal function is the cause of anomalies in the excretion of uric acid and other purin bodies in gout, then a vast literature, which has been built up on the assumption that such excretory anomalies were the result of metabolic disturbances, is incorrect. However, the subject is such a vast one and the problems involved are so complex that it has not been unquestionably proved that renal retention is the only factor concerned in producing a high uric acid content of the blood and low uric acid and purin-nitrogen urinary excretion. It should be stated that all methods for quantitating purin-nitrogen in the urine are inaccurate.

**Uric Acid.**—Studies on the uric acid content of the blood and the excretion of uric acid into the urine have been made in all but 1 case of this series (No. XII). The reports on such estima-

tions made in the blood previous to the recent work of Folin<sup>2</sup> are open to serious question as to their accuracy. This is because Folin reported certain errors in his original method shortly after its publication. But in spite of this report, his original method and modifications of it have been rather widely used. The exact status of the results obtained by the original Folin method and its modifications is not established. This can only be accomplished by comparing such results with those obtained by the recent method of Folin.<sup>2</sup> In as far as this has been done the results obtained have been fully comparable from a clinical standpoint. By using Folin's methods it has been found, in cases of this series, that uric acid in the blood in gout remains persistently at a high figure. The maximum figure for the normal amount of uric acid in the blood probably rarely exceeds 3 mgm. per 100 c.c.

Judging from the findings in this series of cases the estimation of the quantity of uric acid in the blood is of value in the diagnosis of gout. However, it is claimed<sup>3</sup> that uric acid is increased in the blood in the incipient stages of the ordinary types of chronic nephritis. But the methods used in all the work from which this deduction is drawn are subject to the error of giving results which at times are too high. Therefore, whether or not the deduction is justified remains an open question. Nevertheless, until the question is settled *the diagnostic value of a high figure for uric acid in the blood is less than that of a low figure; a low figure is very strong evidence against gout.* In this connection it should be stated that low figures have been reported in gout, but not with the new Folin method. The methods that were used were subject to technical and certain chemical difficulties which could readily lead to error. In interpreting the findings of an increased amount of uric acid in the blood those conditions other than gout in which this is known to occur must be considered. They are nephritis, arterial hypertension, certain acute and chronic types of non-gouty arthritis, chronic lead-poisoning, leukemia, malignancy, acute infections, especially lobar pneumonia.

The accuracy of methods for the determination of uric acid

in the urine are better established than those in the blood. The studies of the author and other workers have shown that in gout there is an abnormally small excretion of uric acid in the urine after the intravenous injection of uric acid or after feeding substances rich in nuclein. Similar findings occur not infrequently in non-gouty persons. *For this reason the data obtained from studies of the excretion of uric acid in the urine are not characteristic enough of gout to be of sufficient diagnostic value to warrant the large amount of work and time necessary to carry them out.*

**Radiographic studies** in gout are of interest. Careful studies<sup>4</sup> of the plates of the hands and feet were made in Cases I-VI, VIII, X, and XIII of this series. The changes found may be divided into the four following groups, which more or less overlap each other:

1. The focal areas of decreased density may be the only changes found. These changes are usually most pronounced in the heads of the metacarpal or metatarsal bones.
2. Besides the focal changes just mentioned, very slight lipping at the margins of the articular surfaces of the bones entering into the first metatarsophalangeal joint occurs.
3. In addition to the changes noted above, there usually occurs either a variable degree of atrophy of all the bones of the affected member or of only the bones of an involved joint.
4. In addition to all the above changes narrowing of certain joint spaces with marked proliferative and atrophic changes occur.

A striking peculiarity of the arthritis is that only certain joints are affected, while others remain normal or nearly normal. A second characteristic is that in almost every case where there are marked changes in a joint the bones entering into its formation show atrophy. This atrophy may be limited to these bones or it may be generalized in the member affected. The cause for bony atrophy, when present, is somewhat problematic. It may be due, in part, to the pressure of the large tophaceous areas in some cases; or it may be the result of lack of use of the affected members, the so-called atrophy of disuse. A third

characteristic is that in the cases in which arthritic changes are present one or both metatarsophalangeal joints of the great toes are involved in the pathologic changes.

Hallux valgus occurs in some of these cases and may explain the arthritic bony changes. In other cases no cause except that of an arthritis due to gout is evident. It should be emphasized that this region of the foot is subject to more or less trauma, but the rôle it plays in producing chronic arthritic changes cannot be ascertained. A striking feature of the arthritis in the cases showing the most marked bony changes is the almost invariable symmetry in the two hands or feet of the bones and joints affected. No relation is ordinarily found to exist between the length of time in which gouty symptoms have been present and the extent of bony changes found in the radiograms. The cyst-like areas sometimes found in radiograms of the bones of gouty patients (Plate 2) are considered to be especially characteristic of gout. Strangeways,<sup>5</sup> McCarty, and the author<sup>4</sup> have shown that types of arthritis occur in patients who clinically are not gouty, but in whom the radiographic changes exactly resemble those found in gout. For this reason there are no *x-ray* findings which are diagnostic of gout. In fact, and contrary to general belief, *x-ray studies are of very little value as an aid in making the diagnosis of gout*. Negative findings are of more importance as an aid in ruling out gout than are positive findings in confirming that diagnosis.

**Irregular Gout.**—There is a large collection of manifestations which are commonly stated to be the result of gout or a gouty diathesis. These manifestations vary all the way from flatulence to arteriosclerosis and from eczema to chronic myocarditis. They occur in the gouty and in those of gouty parentage. Some of them, as arteriosclerosis and chronic nephritis, are commonly observed in gouty persons. In this connection a case reported by Christian<sup>6</sup> is of interest. The patient had been studied for chronic nephritis a considerable time prior to the first attack of podagra. Since no tophi were demonstrable, it cannot be positively stated that the case was one of gout. However, it serves as a possible example of so-called nephritic gout.

in which nephritis precedes the attacks of arthritis. Chronic nephritis was present in 4 of the cases of this series (IV, VII, VIII, and IX). Of the remaining cases, renal function was found to be abnormal in the 6 patients in whom it was studied. Arteriosclerosis and chronic myocarditis were also rather commonly found. These findings suggest the possibility that the manifold manifestations of irregular gout are of a true gouty nature. However, the manifestations of irregular gout occur in non-gouty persons and persons without gouty parentage. This renders the existence of the gouty nature of such manifestations questionable. For this reason there are a certain number of us who limit the clinical entity of gout to a few characteristic symptoms; *i. e.*, tophi and arthritic manifestations as represented by the cases of the series here reported. None of us will deny that manifestations other than these are due to gout. We simply admit that we do not know whether they are or are not.

**Diagnosis of Gout.**—The different types of arthritis which correspond to the typical clinical type-forms are not particularly difficult to diagnose. In actual practice, however, a type-form presents more or less of an admixture of other type-forms; so in a given case it is often difficult or impossible to make a definite diagnosis. There are occasional types of arthritis in which the pain and tenderness resemble that of acute (regular) gout, but which for clinical reasons are not considered to be gouty. In such cases the patient is under thirty years of age, or the blood uric acid is not increased, or the inflammation jumps from joint to joint, as is common in acute rheumatic fever. Such cases may possibly be gout; but this cannot be positively proved in the absence of tophi. Rarely one sees a type of acute arthritis exactly resembling that of gout. The arthritis is limited to some one joint—in the first left metacarpophalangeal joint in one of our cases in which the blood uric acid was not increased—and subsides after a few to a number of hours. The attacks do not recur. These types of apparently non-gouty arthritis make it wise to refuse to diagnose gout positively in the absence of tophi, although all other symptoms of that disease are pres-

ent. But in some such cases it is highly probable that the diagnosis of gout is correct.

The rules for making a diagnosis of gout in this clinic are as follows:

1. *A positive diagnosis of gout can only be made when tophi are demonstrated from which sodium urate crystals are obtained.* This was accomplished in all the cases of the series here reported.

2. *A highly probable diagnosis* can be made when repeated attacks of acute regular gouty arthritis occur and are associated with a uric acid value of more than 3 mgm. per 100 c.c. of blood. These conditions were fulfilled in 11 of the cases reported in this series.

**Treatment.**—Many observers claim a connection exists between diet and the onset of attacks of gouty arthritis. In the few cases in which I have had the opportunity to test this, diet seemed to play no rôle. But because uric acid is usually not properly excreted by gouty persons it seems wise to limit the nuclein intake. This is done by excluding foods from the diet which are rich in nucleins. In the average case without demonstrable nephritis meats, such as beef, mutton, fish, and chicken, are allowable in moderate amounts. When nephritis is present the protein intake will be largely governed by the urea nitrogen content of the blood.

Regular habits of eating and sleeping, together with a large amount of outdoor exercise, and especially the latter, are very beneficial.

Patients should be taught the use of some preparation of colchicum. In true gout an active preparation of this drug acts as a specific. Colchicum bears the same relation to the therapy of gout that digitalis does to myocardial conditions. There is, therefore, no point in discussing other antigout remedies. Three of the patients reported in this series are able to keep themselves fairly comfortable and free from severe attacks by the timely use of colchicum, whereas formerly their existence was miserable. Whenever an attack begins, 0.0006 gm. of colchicum is taken every four hours until the pain is relieved.

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FROM THE MEDICAL CLINIC OF THE MASSA-  
CHUSETTS GENERAL HOSPITAL

**Two Cases with Chronic Gastro-intestinal Symptoms. Com-  
ments on the Use of Transfusion in Pernicious Anemia**

By GEORGE R. MINOT, M. D.

**Certain Types of Pneumonia and Serum Treatment**

By FREDERICK T. LORD, M. D.

**The Diagnostic Value of Electrocardiography of Hearts Beating  
Regularly**

By PAUL DUDLEY WHITE, M. D.

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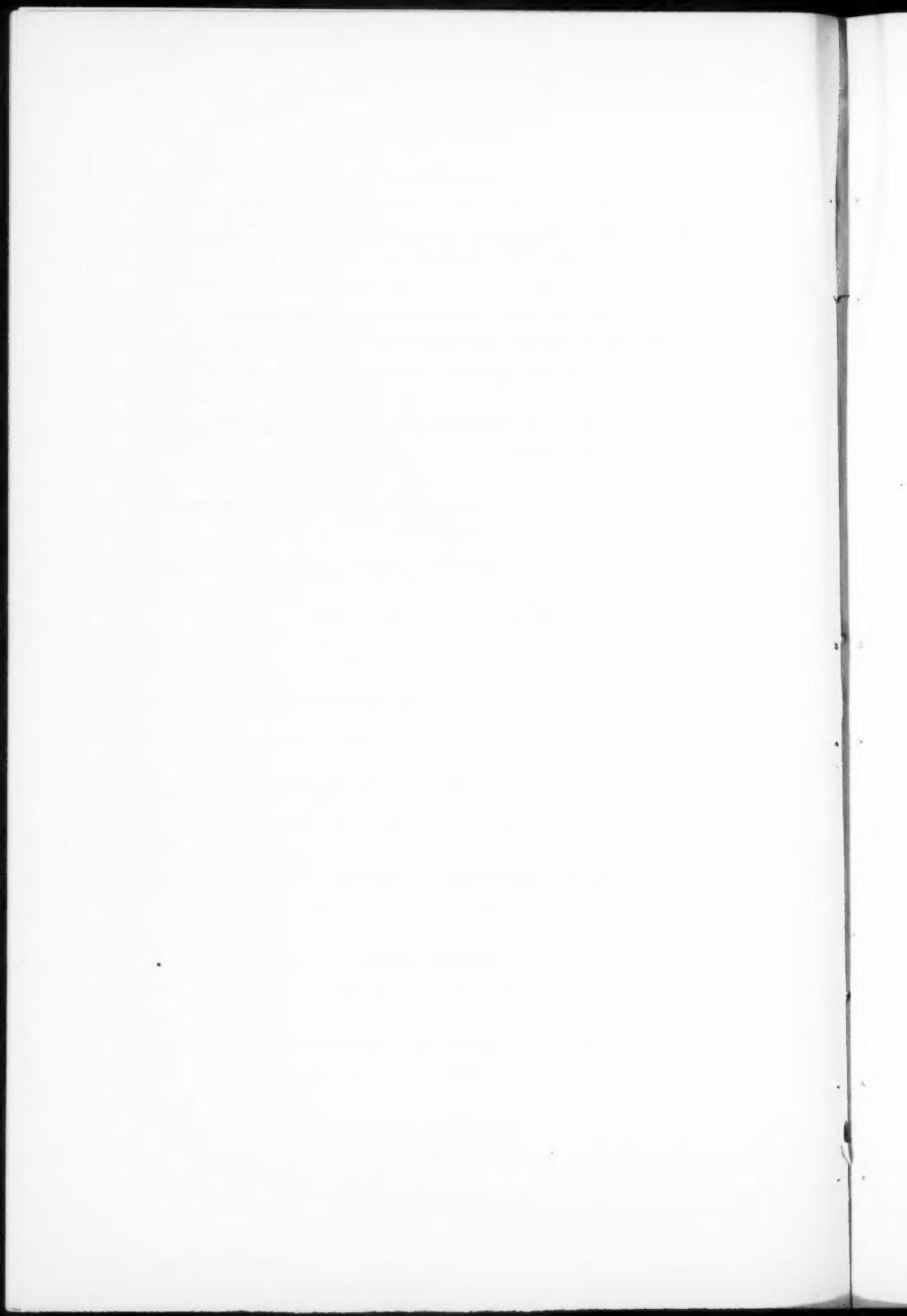
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## CLINIC OF DR. GEORGE R. MINOT

MASSACHUSETTS GENERAL HOSPITAL

### TWO CASES WITH CHRONIC GASTRO-INTESTINAL SYMPTOMS. COMMENTS ON THE USE OF TRANSFUSION IN PERNICIOUS ANEMIA

#### 1. Case of Pernicious Anemia Confused at First with Peptic Ulcer.

The Differential Diagnosis of the Case. Example of How Roentgen Ray Examinations May Be Misleading. Comments on the Tongue and Taste in Pernicious Anemia, the Gastric Analysis, the Loss of Weight in this Disease, its Gastro-intestinal Symptoms, and Some of Those Referable to the Central Nervous System.

#### 2. The Use of Transfusion in Pernicious Anemia.

#### 3. Case of Chronic Intestinal Indigestion.

The Importance of the Stool Examination. The Treatment.

I AM going to show you today 2 patients, both of whom are slightly pale, and have a history of gastro-intestinal symptoms of a rather long duration.

#### CASE I

The first patient is a married man of forty-three years. His occupation is that of clerk.

**Family history** is negative.

**Past history** is negative except for the fact that he has had intermittent headaches for many years, which have been recently relieved by eyeglasses.

**Habits** are entirely normal.

**Present Illness.**—When the patient was first seen in the Out-patient Department two weeks ago he gave the following history of his present illness: Fifteen years ago he first began to have a sense of heaviness in the upper abdomen, which occurred

particularly after his meals. This would be followed by belching of gas and sometimes by regurgitation of food, which completely relieved him. These symptoms have continued more or less constantly ever since, becoming definitely worse in the past three years, but they have never been severe enough to cause him to stop work. With these symptoms he has occasionally had dizzy spells. About a year ago he began having pain in the region of the umbilicus, which has persisted and increased to date. This pain has not been sharply localized. It consists of a dull ache which appears an hour after he has eaten and lasts until about an hour before the next meal. It has been temporarily relieved by soda and by food. He has not been free of this pain for more than a day at a time.

Since he has had the dull pain in his abdomen he has lost his appetite and lost his taste for food. A great deal of the time during the past year his throat and mouth have been sore. This has been severe enough to sometimes bring tears to his eyes, particularly if he takes acid food. There has occasionally been nausea and he has vomited twice. The vomitus has not contained any dark material or bright blood.

The bowels have always moved regularly once or twice a day. The stools have never been light in color, and never tarry. There has been no jaundice.

His best weight was 155 pounds fifteen years ago, while a year ago he weighed 137 pounds, and at the present time 123 pounds.

The only other symptoms that the patient has had are those referable to the circulatory system. About two months ago, following rather severe exercise, he had an attack of shortness of breath accompanied by a non-radiating, dull, precordial pain, with palpitation of the heart. Since then he has experienced slight shortness of breath on exertion.

The physical examination made at that time showed a well-developed and nourished man, with his mucous membranes appearing slightly pale and his scleræ clear. There was no note made concerning his tongue. His eyes, ears, nose, lymph-nodes, throat, tonsils, and lungs were found negative. His

upper teeth were false and about the lower teeth there was some pyorrhea. The heart was not enlarged and it was not found abnormal. The systolic blood-pressure was 120 and the diastolic 80. The abdomen was found entirely negative and no organs or masses were felt. The genitals, reflexes, and extremities were negative. The urine was negative. The hemoglobin was 90 per cent. by Tallqvist's method. No further blood studies were made.

On account of the history this patient gave, taken together with the rather negative physical examination, it was thought that he had peptic ulcer with hyperacidity. On this account a Roentgen ray examination was made of the gastro-intestinal tract, which was reported as follows:

"The stomach shows a small but rather definite prepyloric filling defect and irregularity, no residue, sphincter irregular. The first portion of the duodenum appears to fill normally. Ileum was normal in appearance. Barium occurred in the splenic flexure in six hours, and the cecum normally filled, being perfectly movable and not tender. The appendix was not seen and not tender. The colon was normal in appearance. There is probably a pathologic process in the lower portion of the antrum. It has some of the features of either ulcer or malignancy."

Opportunity for another Roentgen ray examination was asked for by the roentgenologist and was made. The report on this was that the appearance was the same as before and was compatible with either induration from ulcer or a malignant process.

The report of these Roentgen ray examinations substantiated the belief of the clinicians that the patient probably had a peptic ulcer.

The patient now, after a two weeks' interval since he was first seen in the Out-patient Department, has been admitted to the hospital wards for further study. Upon admission to the wards the history was gone over very carefully, and it was found to be as given, except for the following important facts concerning his gastric symptoms, sore mouth, and loss of taste. The

pain in the abdomen of a year's duration has not been as definite in character as previously stated. The facts are that in the past three years the belching of gas has been associated with a good deal of abdominal discomfort that came on without definite relation to meals, while in the past year he has had a dull ache in the upper half of his abdomen that has occurred at no regular time of day, accompanied by some bloating and soreness. Food has not relieved this and soda rather seldom.

We may thus see that the history suggesting peptic ulcer is not as clear cut as it was believed to be. This, as well as the remarks below, serve to emphasize the fact that one must be extremely careful in obtaining the history of a patient, and particularly so when the symptoms are referable to the gastrointestinal tract, because often the correct diagnosis of gastrointestinal disease depends in a very large measure on the history.

Further inquiry regarding his sore mouth gave the following information: He knows that he experienced a sore tongue at least three years ago. However, it did not become particularly bothersome until a year ago. During the past year the soreness of his tongue has occurred periodically for days at a time, being practically free of it for periods of days and sometimes weeks. This soreness has particularly occurred at the tip and edges of the tongue. With the soreness of his tongue he usually has had soreness about his whole mouth. Sometimes it has been so sore that if he took acid foods he would cry out with pain. He also tells us that his taste has been lost to such an extent that he can only tell whether the food is definitely sweet or definitely sour. Tests have shown that he has a distinct diminution of his sense of taste. With the loss of his sense of taste he has also lost his appetite.

The complete physical examination in the wards has revealed nothing different from what was noted in the Out-patient Department except that his tongue appears smooth and shiny and the papillæ are much less prominent than normal. The tongue is somewhat meaty in appearance and superficial ulceration is evident on the tip and edge, while occasionally tiny vesicles appear about the tip.

The following laboratory examinations have been negative—the urine, stool, and Wassermann reaction on the blood.

With this history of recurring soreness of the tongue the most important laboratory examination that can be made is that of the blood. This is because the tongue symptoms that this individual presents are typical of pernicious anemia, and very rarely do periodic tongue symptoms of this nature occur in other conditions. It is quite typical for this disturbance to be particularly confined to the anterior half of the tongue. The appearance of his tongue is also typical, namely, the raw, red, beefy appearance and the superficial denudation of epithelium, as well as its atrophic appearance. When the tongue is not painful, commonly one will see in cases of pernicious anemia that it appears simply atrophic, flabby, shiny, and smooth. One should not forget that in fully 45 per cent. of the cases of pernicious anemia the patient will have subjective disagreeable sensations referable to the tongue and mouth some time during the course of the disease, and more commonly relatively early than late.

It is easy to forget that tongue symptoms of this nature occur in pernicious anemia, and not infrequently individuals with this disease will have other symptoms that are more prominent, and they will forget to mention that they have or have had tongue symptoms, so that when one suspects this disease questions should be asked directly referable to the condition of the tongue and mouth. A history of a recurring sore tongue alone should give a most important clue to the diagnosis.

The loss of taste that this patient has appears to be at least partially due to atrophy of the taste papillæ, and this state of affairs too, though unusual, seems to be of not a very rare occurrence in pernicious anemia.

With the suspicion of pernicious anemia as the diagnosis of this individual's disease let me tell you what the examination of his blood shows.

The hemoglobin, determined by the Palmer method, is 85 per cent. The red count is 2,660,000. The color index is thus distinctly high. The red cells show a definite and distinct gen-

eral macrocytosis and the cells take the stain deeply. They are commonly oval in shape, and though variation in shape occurs, it is not at all marked. A considerable variation in size is evident, but this is also not marked, a feature being that a few true microcytes occur, though the vast majority of the cells are larger than normal. Polychromatophilia occasionally occurs. Stippling, blasts, and other abnormalities are not present. The reticulated red cells, which are young red cells, are  $1\frac{1}{2}$  per cent.

The white count is 5600. The differential count is:

Polynuclear neutrophils,	67	per cent.
Polynuclear eosinophils,	3	"
Lymphocytes,	27	"
Large mononuclears,	3	"
	100	"

The white cells are of normal types.

The blood-platelets are definitely but slightly diminished.

From this blood examination you may see that we have a blood-picture that is typical of pernicious anemia, namely, a high color index, a general macrocytosis with the presence of microcytes, diminished platelets, with non-elevation of the white count.

It is to be learned from this blood examination that a routine examination of the hemoglobin alone may not lead to a further examination of the blood. One of the things that may surprise you is the fact that this patient looks but slightly pale and has been constantly at work, yet his red count is but 2,660,000. You, however, should not forget that there is no other disease than pernicious anemia which so often reduces the erythrocytes below 2,500,000, and that frequently the count will reach such a level in this disease before the individual feels sick enough to consult a physician. Thus a patient with anemia feels well more in proportion to the percentage of his hemoglobin than in proportion to the number of his red cells.

Cases of pernicious anemia commonly appear yellowish, but this patient does not appear yellow, though, with his slight pallor, he does appear a trifle sallow. The yellow color that pernicious

anemia patients have is dependent upon an abnormal amount of blood destruction, but such a color may not be at all evident when abnormal blood destruction is occurring. Abnormal blood destruction is one of the features of pernicious anemia. The other feature of the blood is the abnormal blood formation.

I will not discuss with you the tests for blood destruction, but they show that this patient has a definite abnormal increase of blood destruction.

The fact that this patient presents the tongue symptoms so characteristic of pernicious anemia and has a blood-picture characteristic of this disease, but not wholly diagnostic of it, taken together with the fact that he has evidence of blood destruction, practically makes the diagnosis of pernicious anemia. If this is the case, how are we to explain the Roentgen ray findings of ulcer or malignancy? Further Roentgen ray studies were made, with the following report based on two more examinations: "The stomach shows no filling defect. Several peristaltic waves appeared to pass completely over the antrum. The sphincter was not definitely made out. The duodenum was normal. No definite lesion was found."

We now have a contradictory report from the former reports, but Dr. Holmes tells us that the first Roentgen ray findings may have been due to improper judgment or may be explained by spasm of the pylorus, and that it is not necessary to presume that a lesion is present by such a finding alone. He feels that the last examinations have been more satisfactory than the first, and represent much more probably the actual state of affairs. By this Roentgen ray examination we have removed some of the evidence of ulcer that we previously had, while by reviewing the history, which is entirely consistent with pernicious anemia, and taking into consideration the patient's tongue symptoms and the blood examinations, a diagnosis of ulcer becomes very unreasonable and impossible unless two diagnoses are made, so that the diagnosis of pernicious anemia is established. We have not as yet discussed why a diagnosis of malignant disease of the stomach may not be made, but I will take that up later.

The varying Roentgen ray reports serve to emphasize the

well-known important fact that a diagnosis should not be made from the Roentgen ray examination alone, and one must be careful to not be led astray by a Roentgen ray report, as perhaps occurred in this case.

Before it was possible to study the gastro-intestinal tract by means of the Roentgen ray a great deal was learned from the study of the gastric contents, but today this method of studying gastro-intestinal cases is frequently neglected owing to the belief by some that the Roentgen ray will give all the information desired. This method of studying the condition of the stomach should not be neglected, and in this case it gives us important information. The gastric analysis was found to be as follows:

Fasting contents 10 c.c. of bile-colored watery material.

Free hydrochloric acid absent.

Total acidity 0.1 c.c. decinormal sodium hydrate.

Microscopically no abnormalities noted.

The test for occult blood was negative.

Test-meal—25 c.c. of normal-appearing material.

Free hydrochloric acid absent.

Total acidity 0.5 c.c. of decinormal sodium hydrate.

These tests show that there is an absence of free hydrochloric acid in the stomach and that the total acidity is very low. These are unusual findings with ulcer of the stomach, which condition is commonly associated with an increased amount of acid.

Thus we have one more bit of information that leads away from a diagnosis of ulcer and a bit of information that should lead toward the diagnosis of pernicious anemia. This is because it is quite characteristic for cases of pernicious anemia to have achlorhydria and often achylia. This feature remains present whether the individual is in a state of remission or relapse, and it may be one of the first indications of the disease that will be found. It apparently may be present for some years before any definite anemia or any clear-cut blood changes are observed. Cases not showing achlorhydria should be diagnosed cautiously as cases of pernicious anemia, because practically all cases of pernicious anemia exhibit this feature. When

a diagnosis of gastric carcinoma is suspected the absence of free hydrochloric acid is corroborative evidence of this condition, as it is when pernicious anemia is suspected, but this finding is only present in a moderate number of cases of carcinoma, while it is rare to find the acid present in cases of pernicious anemia.

A further test has been done by Dr. Loeb on the stomach contents of this patient. This is the Wolff-Junghans' test. This test consists of taking the fasting contents free from hydrochloric acid and blood and mixing it thoroughly with distilled water, from which dilutions of from 1 to 10 to 1 to 400 are prepared. To these solutions, which are first filtered, are added 2 drops of Wolff-Junghans' reagent.<sup>1</sup> This reagent permits albumin rings to form. When they occur only in the lower dilutions, it appears to indicate that the achlorhydria is benign rather than the result of malignancy, while when albumin rings are present in the much higher dilutions (1 to 200) malignant disease is very probable but not certainly present.

This test applied to this patient's stomach contents showed that the albumin rings occurred in no greater dilution than 1 to 80. Thus this test, which is not infallible, strongly favors the diagnosis of benign achylia in this case, rather than one associated with malignancy.

You will recall that this patient has experienced a loss of 32 pounds in fifteen years and 14 pounds in the past year. Some of this loss of weight may be explained by the fact that he has had a diminished food intake, and we learn, upon questioning him rather closely, that with his poor appetite the total amount that he has taken has been distinctly less than he is accustomed to.

A point that I wish to emphasize to you is that cases of pernicious anemia do lose weight and do so not uncommonly, and that some, though not all, of the loss is dependent upon the eating of too little food. I wish to emphasize this because of the fact that it is incorrectly commonly said that loss of weight serves as a crucial point in distinguishing pernicious anemia from gastric cancer. In about 40 per cent. of the cases of per-

<sup>1</sup> Jour. Amer. Med. Assoc., 1915, vol. II, p. 836.

nicious anemia a considerable loss of weight occurs. It may occur with relapses, to be regained in remissions, but variations in weight are not by any means parallel to the red count.

You have probably heard that the blood-picture of pernicious anemia may occur with carcinoma of the stomach, and you may perhaps wonder why this case is not one of this disease. It is true, of course, that carcinoma of the stomach commonly gives rise to a simple chronic anemia of the so-called secondary type, and this may be a very severe grade, while rarely the blood-picture seen with carcinoma of the stomach at a time when there is a marked reduction of both the hemoglobin and the red count may give a startling resemblance to that seen in pernicious anemia, but *not* when the hemoglobin is as high as in the case before you. If one carefully scrutinizes the blood-picture in these uncommon instances, it will usually be found to differ from that ordinarily seen in pernicious anemia, though rarely it may be difficult to do so. In such instances tests for blood destruction are valuable because they will show considerable increased destruction with pernicious anemia, and apparently will not be significantly abnormal with cancer.

Thus the blood-picture this patient presents, taken together with the level of hemoglobin and red count and the presence of abnormal blood destruction, is not what occurs with cancer of the stomach. Also the tongue symptoms which this patient has do not occur with cancer; while from the physical examination there is no evidence of a gastric lesion, nor is there from the Roentgen ray examination. Likewise, the absence of occult blood in the stools or stomach contents as well as the Wolff-Junghans' test is against malignancy. From the history alone you might suspect malignant disease beginning at the time the gastric symptoms increased about a year ago, but all the gastric symptoms cannot be explained by this cause, owing to their long duration. We thus have no evidence of malignancy and plenty of evidence for the diagnosis of pernicious anemia.

In relation to the diagnosis of pernicious anemia I have not as yet commented on the rather long history of gastric symptoms that this patient has had, and I will do so now. The gastric

symptoms that this patient has had are entirely like those that many cases of pernicious anemia have. In fact, practically every case of pernicious anemia has symptoms referable to the stomach or intestines at some time in the course of his disease. These symptoms would appear to be dependent upon, in some instances, actual atrophy of the mucosa, while simple atony dependent upon diminished blood-supply may be the cause in others. In still others they may be dependent upon improper secretion of the gastro-intestinal juices, while not infrequently the cause is not clear.

The symptoms occurring in pernicious anemia that are referable to the stomach and intestines are loss of appetite, nausea, vomiting, and diarrhea, paroxysms of which are more or less prominent. At times there is diarrhea alternating with constipation, while in some instances constipation alone is prominent. Indefinite abdominal pain, with a sense of fulness, pressure, and distention, not infrequently associated with the passage of an excessive amount of gas and putrefactive stools, commonly occurs. It is not at all uncommon to see periodicity of the gastro-intestinal symptoms similar to the periodicity of the tongue symptoms, so that periods of good digestion will alternate with periods of bad. The periods of bad digestion do not necessarily coincide with a falling red count, the hemoglobin percentage or the degree of increased red cell destruction, though they are more apt to occur when the former is lower and the latter greater. It does seem that such symptoms are frequently related to the blood volume. They appear to be severer when the volume is less, and with their increase the volume diminishes still more, and until the volume is increased either by nature in some manner or by artificial means the symptoms persist.

Cases of pernicious anemia having a history of gastro-intestinal disturbances for some years, even as long as twenty-five years, before they become definitely pale, are not unusual, and are commonly not diagnosed until the anemia becomes most evident. Such cases may take on features that suggest organic gastric or intestinal disease. There are some cases of pernicious anemia that have attacks of sharp epigastric pain

severe enough to double the patient up, associated with vomiting. Attacks of this nature may resemble the gastric crisis of tabes dorsalis, and some such attacks may resemble them closely, because they are due to a similar cause, namely, degeneration of the central nervous system.

Cases having relatively little anemia and prominent, rather long-standing gastro-intestinal symptoms are commonly diagnosed—as was this patient—some type of chronic primary gastro-intestinal disorder. Such cases have been operated on for chronic appendicitis, duodenal ulcer, etc., and the surgeon has been disappointed in not finding any definite pathology. In some such cases the blood-picture is not clear cut and demands careful, critical study, but the correct diagnosis can be made if the case, as a whole, is carefully studied. One should thus not forget that in the differential diagnosis of chronic gastro-intestinal disease pernicious anemia is to be always thought of, and that though the symptoms may be periodic in nature, there often will be a history of continuous gastro-intestinal symptoms with or without temporary increase in the symptoms, which temporary increase may be at times of a severe type.

The dyspnea and palpitation that this patient has complained of is readily explained by the anemia. Such symptoms will occur from anemia of any type because of a diminished amount of hemoglobin available for carrying an oxygen supply fully sufficient for the needs of the body.

In this connection one should not forget that symptoms referable to the circulatory apparatus are sometimes the first ones of which a patient with pernicious anemia complains. When such is the case, other features of the disease will be present if looked for, though not uncommonly one finds that the diagnosis of primary cardiac disease has been made.

The heart of pernicious anemia patients shows fatty degeneration and presents a tiger-lily-like appearance. Actual cardiac hypertrophy of a considerable degree sometimes occurs in this disease. The physical signs that these hearts present are those of myocardial weakness. Besides systolic murmurs associated with the anemia and dilatation of the mitral valve, diastolic

murmurs may occur, dependent upon the dilatation of the aortic valve.

In summary, it may be said that we can account for all of the abnormalities noted in this case by the diagnosis of pernicious anemia; that the tongue symptoms, achlorhydria, and the blood findings, including those of blood destruction, are typical of the condition.

I will not discuss the prognosis of this case, as it involves more time than we have at our disposal.

Besides periods of ill health (relapses), followed by periods of relatively good health (remissions), which state of affairs is a feature of pernicious anemia and which this patient has not had as yet, there is another feature of pernicious anemia that is common, and that also is not presented by this patient, namely, symptoms referable to degeneration of the spinal cord. Symptoms of this character may lead one to the diagnosis of pernicious anemia in the same manner as tongue symptoms. It is much more common to have relatively trifling symptoms referable to degeneration of the spinal cord, such as slight disorders of sensation, as numbness and tingling of the hands and feet, than those due to a marked degeneration of the spinal cord, when the symptoms are commonly those of a combined sclerosis.

Cases of other forms of anemia may exhibit such symptoms, but it is distinctly rare to find these symptoms marked and persistent in other anemias than pernicious anemia, and then only when the anemia is severe; while pernicious anemia patients commonly exhibit such symptoms when the anemia is slight. It is not at all uncommon if one is on the lookout for cord symptoms to find them early in the disease, particularly in older individuals. In fact, they are nearly always present when the disease occurs in individuals over fifty-five years of age. Commonly the patient will not spontaneously complain of such a disturbance, because some other disturbance will be more prominent, and these nerve symptoms which may give a clue to the diagnosis will be learned only upon asking direct questions. Woltmann recently found in 150 cases of pernicious

anemia indisputable evidence of destruction of the nerve parenchyma in 80 per cent., while 12 per cent. of his cases saw a physician purely on account of the nerve symptoms. These symptoms may dominate the picture and the red count never go very low, while the individual may die of the cord changes rather than of the anemia. Such symptoms do not by any means indicate that death is not far off, and many cases will have them for some years without their progression.

Though nerve symptoms may be the first ones of which the patient complains, it is more common to have definite anemia precede them than for anemia to follow them. Even so, I wish to call your attention to the fact that individuals who present persistent paresthesia of the hands or feet may be cases of pernicious anemia, and that from these symptoms, like the tongue symptoms, a clue may be given to the diagnosis.

#### THE USE OF TRANSFUSION IN PERNICIOUS ANEMIA

Though I do not wish to discuss the treatment of pernicious anemia, or of this particular case that I have just shown you, I do wish to take this opportunity to simply comment upon the use of transfusion in this disease. This method of treatment is to be looked upon as one of our methods of helping individuals with pernicious anemia, but it is not to be looked upon as the one and only thing that should be done. Rest, fresh air, proper forced feeding, care of the digestive tract, removal of foci of infection, etc., are important and are not to be lost sight of.

Transfusion in pernicious anemia never cures the disease and does not prolong life to any significant degree. Transfusion may be employed in relapses to relieve symptoms and with the hope of bringing about a remission. It appears to give more constant remissions than any other form of therapy that may be commonly used. It is possible, however, to parallel the most marked remission following transfusion with a case that has had no such treatment. The chances of a spontaneous remission occurring when a case is seen in a relapse is in the vicinity of 35 per cent. Transfusion in pernicious anemia appears to bring about 10 to 20 per cent. more remissions, dependent upon some-

thing more than simply filling the patient up with blood, than occur spontaneously. In selected cases the chances of a remission are probably greater. The duration of remissions aided by transfusion is in nowise different from the spontaneous remissions.

No case is too sick to receive a transfusion, but if one decides to transfuse, it should preferably be done before the blood volume, red count, or hemoglobin becomes extremely low, and one should not wait until the patient has been in a state of relapse for many weeks. It would seem desirable to keep the patient above the level of a severe anemia, in view of the fact that anemia *per se* is deteriorating to the various organs of the body, and by so doing one may perhaps induce remissions at a later date that cannot be induced at the time. It is probably wise not to transfuse at the time of acute hemolytic crisis.

The type of cases that are apt to receive the most benefit from transfusion are the same as those most apt to have spontaneous remissions and that have the best course of the disease without transfusion. Patients who have had or may be expected to have definite remissions receive the most benefit, so that a careful study of the blood factors and a clinical study of the patient will often tell what is to be expected from this procedure. It is not my purpose to discuss here the types of cases in which remissions are apt to occur or how one may judge the chances of remission from the state of the patient, the blood findings, or other laboratory data.

It is certain that transfusion for pernicious anemia is not to be used promiscuously and every time a case is seen in a relapse, because it cannot by any means always do good except perhaps in a very temporary manner. For example, in an elderly case that has had a prolonged downward course with slight remissions for a period of two years, one cannot expect—though it may occur—more than slight temporary benefit from transfusion, and in such an instance it cannot be urged or perhaps really advised. On the contrary, with a young individual seen at the time of his first marked relapse transfusion repeated several times is to be urged. Thus, one must weigh the chances

of remission from the clinical state of the patient, as well as from the laboratory evidence of the degree of activity of the marrow and the degree of blood destruction, when deciding to urge or to do transfusion in these cases. The patient's wishes and those of his family also must be taken into consideration when deciding to do transfusion in pernicious anemia.

One transfusion from a proper donor and properly done is often to be advised in any relapse, as it can do no harm, but according to the condition of the patient as alluded to may be urged or given in the spirit of simply trying to do something for the patient and his family. When the result of one transfusion is followed by evidence of definite improvement that appears to depend upon more than purely the presence of foreign blood, a second one is often to be advised seven to fourteen days later; sooner if serious blood volume reduction or low counts are present. If rapid improvement is occurring, a second one may be postponed, while with improvement more may be given to hasten the remission and improve its degree. In relapses, where the first transfusion gives no evidence of distinct improvement, a second and third may be tried, but sometimes they will not yield significantly better results. Several transfusions, however, are to be tried when one considers the patient a type of case that should improve. It is a fact that two or three transfusions at one time may yield no noteworthy remission, while they may at another time, or the patient spontaneously at a later time may have a good remission. Such a state of affairs is unusual. Anders recently, in reviewing the literature, has found that of 362 cases receiving transfusions at the time of a relapse, an average of 2.4 transfusions were given each patient, and that relatively small (500 c.c.) transfusions were usually given. It seems that the best gains, and thus better remissions, have been reported when repeated transfusions giving a total large amount of blood were used. The benefit in some such instances is probably wholly dependent upon the life of the transfused red cells, though in others it appears to hasten the onset of a desirable remission quicker than when lesser total amounts of blood are used. If plenty of donors are available and one feels

that the patient wishes to be simply filled up with blood and live as comfortably as he can on the foreign blood, transfusion may be done more often than when one aims to use transfusion to initiate a remission sustained by the patient's own blood; but initiated at an increased rate with a better degree of improvement than usually occurs spontaneously.

From this discussion some may derive an unfavorable aspect of transfusion in pernicious anemia. However, it is the one procedure that can be successfully employed to relieve symptoms in these patients, except those definitely referable to changes in the central nervous system. It is also to be noted that frequently following relief from one transfusion the patient requests another, so that often they may have to be given to keep the patient comfortable, though as a chronic invalid. Though such may be the case in some instances, we must realize that transfusion is a very valuable procedure in others. Many cases treated in such a manner are more likely to show constant temporary improvement and be more comfortable while they live than without such treatment. The availability of donors, the state of the patient, and his wishes, determine when to transfuse and whether to repeat the procedure.

#### CASE II

The second case is a married man, forty years of age, a manufacturer, who gives the following history.

The **family history** and the **past history** are negative.

His **habits** are good except for the fact that he takes no exercise, not even walking to his office, and that he works very intensely, without holidays.

**Present Illness.**—The patient states that what he seeks relief for is that for the past six months he has constantly "felt tired," that he has been "unable to think clearly," that he "has no energy," but that he has no other symptoms except some "indigestion," which he has had a long time. He tells us that the indigestion does not particularly bother him, and that if the other things he suffers from should vanish he would not be disturbed by his indigestion. He cannot recall exactly when his

indigestion began, but he has apparently had it for about eight years. It consists of an indefinite abdominal discomfort associated with a bloating sensation throughout his abdomen. The discomfort is worse on some days than on others, but he has not been free from it for more than a few days at a time. The discomfort apparently does not occur at any definite time of day nor is it affected by food. There has been no vomiting and rarely nausea. There has been no jaundice and no sharp pain. He rather commonly passes a considerable amount of gas by rectum, but relatively seldom belches any gas. His bowels have been regular, without catharsis, moving once and sometimes twice a day. The stool is usually soft and seldom well formed, though previous to ten years ago he always had formed stools. His indigestion has been rather more evident in the past six months since he has felt tired, and he attributes the increase of his abdominal symptoms to his sense of fatigue. There have been no other symptoms than those noted.

**Physical Examination.**—The man is of a rather slender build, with flabby muscles and a rather drooping posture. He looks tired and slightly pale. The abdomen is entirely negative except for the fact that it is slightly distended with gas. The rest of the complete physical examination is wholly negative.

The urine is negative.

The **blood examination** shows as follows: Hemoglobin, 80 per cent.; red count, 4,800,000. The red cells show slight achromia and slight variation in size, and they present no other abnormality. The white count is 9000. The differential count is not abnormal. The blood-platelets occur in normal numbers.

There is no evidence of excessive blood destruction.

In contrast to the first case, the hemoglobin is slightly lower, but the red count much higher, and the red cells but slightly abnormal in their appearance. The blood-picture is that of a very mild simple chronic anemia, which is commonly called secondary anemia, because it is dependent upon a recognized cause, which in this case is the diseased condition referred to below. From the hemoglobin alone we have learned no more about the blood of this patient than we did about the blood of

the first case, but from the complete blood examination we have learned that we are dealing with a much simpler state of affairs.

The **stool examination** gives us information of the greatest importance. Several examinations of the stool made about three hours after passage have shown it to be always of the following nature: A soft, mushy, dark brown stool, with a definitely foul, acrid odor, giving a strong acid reaction. Many bubbles of gas occurred intermittently mixed with the stool, so that upon stirring it with a stick it crackled. Microscopically, no definite abnormalities were noted. The test for occult blood was negative.

From the simple procedure of looking at this stool and noting its character we see that we have a stool resulting from intestinal fermentation. The normal stool should not be foul nor be strongly acid, and it is not normal for gas bubbles to be present in a stool three hours after its discharge. Normal stools do not form at the most more than a few gas bubbles, even after they have stood for twenty-four hours, and usually no gas bubbles form in this amount of time. If this stool was shut up in a closed jar for a few hours a marked amount of gas formation would occur, so that upon opening the jar there would be a slight explosion.

There is no need for further studies to be made on this case, for with the history of indigestion of the type that he has had, taken together with the acid type of stool, without excess of fat or its derivatives, that is present, we may make the diagnosis of chronic intestinal indigestion, particularly dependent upon defective digestion of the carbohydrate food. As a matter of fact, he has had Roentgen ray examination of the gastro-intestinal tract which has been pronounced negative except for some slight ileal stasis. Examination of the fasting contents of the stomach and a test-meal have shown no important deviation from the normal.

Cases of chronic intestinal indigestion passing a foul acid or alkaline stool, or stools that are simply foul with a neutral reaction, are common, and this condition may occur in individuals

with some other disease, as arthritis, which other condition may be benefited by treatment of the intestinal condition. Cases of pernicious anemia, among other conditions, may have such a disturbance.

In making a diagnosis of intestinal indigestion alone, one must be careful that there is no other disease present. It is not uncommon that patients with intestinal indigestion will complain, as did this patient, less of their indigestion than of their general ill health, which is, of course, largely dependent upon a constant improper digestion of food, though when fatigue occurs the intestinal symptoms are commonly aggravated. Contributory causes to this man's condition are his deficient exercise and chronic fatigue from overwork, while his somewhat drooping posture acts to intensify his ill health.

You should not forget that many times a study of the stool by simply noting its gross character will tell you a great deal about your patient and lead to a definite form of treatment that alone will distinctly benefit many cases. This treatment consists of having the patient take a suitable diet. Various medicinal measures may be helpful adjuncts in the treatment, but proper diet is the main thing that will cause improvement.

This case should be given a diet that consists of just sufficient calories to meet the demands of the body, particularly avoiding the more easily fermentable carbohydrate foods. It is not necessary or desirable that he be kept in a hospital. The following directions may be given to this patient:

Never eat more than is just sufficient to satisfy your desire for food, but do not go hungry.

Eat slowly five small meals a day rather than three large ones, and observe the following rules:

Take 3 or 4 pieces of Zweibach or Swedish bread a day, but no other bread or bread-like foods.

All cereals and cereal, bread-like, or cornstarch puddings are to be avoided, as are cakes and doughnuts and all forms of pastry.

Take no potato, rice or macaroni, or foods containing these, as hash.

No sugar should be taken and no foods that are distinctly sweet, such as honey, jellies, chocolate, candies, syrups, etc.

No flour dressings, rich sauces, spiced or salted foods are to be taken.

All fresh vegetables except corn and onions may be taken freely, but peas and shell beans only very moderately, and baked beans not at all.

Simple salads with French dressing are desirable.

Butter is to be taken freely and may be mixed with vegetables.

Fruits are desirable, preferably cooked, as apple sauce, prunes, stewed pears, etc., without syrupy sauces. Raw apples are not to be taken.

One or two eggs may be taken daily and a moderate portion of fish.

Pork is to be omitted, but bacon may be taken every other day. Beef and lamb may each be taken once a week, while chicken may be taken four times a week.

Thin fresh vegetable and meat soups are permissible, but thick soups are to be avoided.

Two glasses of milk a day are permissible, while cream and cream cheese may be taken. The heavier cheeses should be avoided.

Foods not included in this list may be taken, but no one food not included on this list is to be taken oftener than once every other day.

If this patient follows this diet his digestive symptoms will probably improve, and with their improvement the symptoms which bother the patient the most, which are at least partially dependent upon his digestive disturbance, will probably diminish. After some weeks a more liberal diet may be given, though the more easily fermentable carbohydrate foods should be kept at a minimum as long as possible. The patient's weight should be followed, and he should not be permitted to lose more than a few pounds.

Though a diet of the type outlined is the chief treatment for this patient, he will improve probably quicker and better if he takes more exercise, works less, and avoids fatigue. Definite

setting up exercises are also important to give him a better posture and to enable his organs to functionate more normally. In some cases with intestinal indigestion but little improvement will occur unless the individual's living habits and posture are corrected at the time he is put on a diet.

In concluding this clinic I wish you to note that upon contrasting this last case with the first case that both present slight pallor and a rather long history of ill-defined abdominal discomfort. In the first case the abdominal symptoms are primarily dependent upon a fatal disease of the blood, pernicious anemia, and yet the hemoglobin is higher than in the second case, where the blood disturbance is simple and very mild and dependent upon chronic intestinal indigestion, as particularly told by simply observing the stools. However, as I have shown you, these 2 cases are entirely different, and only resemble each other very superficially.

CLINIC OF DR. FREDERICK T. LORD

MASSACHUSETTS GENERAL HOSPITAL

**CERTAIN TYPES OF PNEUMONIA AND SERUM  
TREATMENT**

**Full Description of Technic and Details to be Observed in Serum  
Treatment.**

THE following case history presents certain features of interest and importance in connection with the different types of pneumonia and serum treatment. The essential facts in the patient's story, taken October 11, 1919, are as follows:

Mr. X. Y. Z., a business man, aged sixty-four, with a negative family and past history and good habits, was operated upon under local anesthesia for an infection in the right antrum eighteen days ago, with the evacuation of about 1 dram of pus. According to his story the antrum was punctured through the nasal cavity. The antrum was probably approached through the inferior meatus (Mikulicz's operation). It was subsequently irrigated every other day, with the evacuation of a diminishing amount of pus. No cough or other symptoms were present during this period. The antrum was apparently well at the onset of the following symptoms:

Four days ago he had a severe shaking chill, nausea without vomiting, and fever. Three days ago he was again nauseated and was found to have a temperature of 100° F. Two days ago his temperature was 102° F. and he began to cough, raising a small amount of rusty sputum. There is no history of pain in the chest. The cough and rusty sputum have continued since.

Examination shows a man of large frame and well nourished, both pale and cyanotic. The skin has a slightly icteric color. The tongue is coated. The lungs show an area with signs of

consolidation in the right back involving the lower lobe, with the exception of a narrow strip about two fingers in width at the extreme base. There is also an area of consolidation in the left back inside the angle of the scapula about the size of the palm. The heart presents nothing noteworthy except that the rate has been slow—about 40 to 50—all his life. The rate is now 80. The respiration is 22. The abdomen, genitals, and extremities show nothing abnormal. Blood-pressure is 100/60. The white count is 16,000. The urine shows a very slight trace of albumin, specific gravity 1030. Sugar and bile are absent. The sediment contains an occasional granular cast. A specimen of rusty sputum shows Type I pneumococcus. No tubercle bacilli are found.

DR. LORD: The patient has a pneumonia. What shall we say as to its type?

STUDENT: Bronchopneumonia.

DR. LORD: Why?

STUDENT: The pneumonia followed an infection of the upper part of the respiratory tract and was of rather insidious onset without pain in the side and with slow rise of temperature.

DR. LORD: Bronchopneumonia usually follows an upper tract infection, but lobar pneumonia also not infrequently follows an infection of the upper parts of the respiratory tract. A history of "cold" followed by cough and expectoration preceding the onset can be obtained in 25 per cent. or more of the cases. It is to be remembered that the onset and course of lobar pneumonia in persons at the patient's age are likely to be atypical. What bearing on the kind of pneumonia has the finding of Type I pneumococcus in the sputum?

STUDENT: The finding of Type I pneumococcus suggests lobar pneumonia.

DR. LORD: The fixed types of pneumococci are present in about 80 per cent. of all lobar pneumonias, while Type IV is found in the remaining 20 per cent. The finding of Type I pneumococci may be used as an argument in favor of the presence of lobar pneumonia, but clinical and postmortem studies have shown that the fixed types of pneumococci singly or com-

bined with other organisms may also be found in a small proportion of cases of bronchopneumonia. It is not possible in this case to come to a definite conclusion as to whether he has lobar or bronchopneumonia, but the onset with chill, rusty sputum, extensive consolidation, and the Type I pneumococcus in the expectoration suggest lobar rather than bronchopneumonia.

The antrum operation eighteen days ago raises the question whether the pneumonia may in any way depend on the operative procedure. The operation, however, was done under a local anesthetic, and there is nothing in the nature of the operation or the history to suggest that it was in any way responsible for the pneumonia. Postoperative pneumonia is a well-defined type. It is important especially because a knowledge of its causes will to a considerable degree prevent its occurrence. It is, unfortunately, not uncommon, and I happen to have seen 4 cases of postoperative pneumonia in the past ten days. About one-quarter of all deaths following operations are due to pulmonary complications, and of these pneumonia is the most frequent. The pneumonia usually begins within the first twenty-four to forty-eight hours of the operation. In a considerable proportion of the cases the pneumonia arises in consequence of operation upon a patient who has or is recovering from a "cold." The pulmonary infection is usually due to the irritation of the respiratory tract by the general anesthetic or the aspiration of bronchial excretion during narcosis. It may also occur in consequence of the aspiration of vomitus or defective inspiratory excursion of the lung in the postoperative period when the patient remains undisturbed for long periods in one posture. It should, therefore, be an invariable rule to make inquiry concerning any recent nasal infection, tonsillitis, or cough, and postpone operation in other than emergency cases until the infection has wholly subsided. The stomach should be empty before operation and the posture should be changed at intervals after operation. Deficient excursion of the diaphragm may follow abdominal operations under local as well as general anesthesia, and, though safer, local anesthesia does not wholly prevent the

development of pneumonia. In urgent cases where operation is imperative, local anesthesia, gas-oxygen, or chloroform are to be preferred to ether. But to return to the patient, what should be the treatment in this case?

STUDENT: The use of Type I antipneumococcus serum.

DR. LORD: What is the evidence in support of this method?

STUDENT: It is said that there is a striking improvement in the general condition following the administration of homologous serum in Type I infections. The local lesion ceases to extend. The septicemia is usually checked. Immune bodies appear in the blood and the mortality from this type of infection is diminished.

DR. LORD: Spontaneous recovery from pneumonia may be ascribed to two factors. In the first place it may be regarded as due to the development of what is known as humoral immunity, during the course of which protective substances are formed in the body of the infected individual. In pneumonia it may be conceived that these humoral factors serve to localize the infection in the lung, prevent its extension into new territory, and check the pneumococcus septicemia. A second matter of importance is the biochemistry of the pneumonic exudate of such a nature that proteolytic enzymes are set free from the cells, a local change of reaction probably takes place, the pneumococcus undergoes dissolution and death, and crisis occurs.

The natural powers of resistance in the elaboration of protective substances against Type I pneumonoccus may be assisted by the intravenous injection of serum derived from a horse whose immunity to the pneumococcus has been raised by increasing doses of the homologous organism. The serum from a horse thus repeatedly inoculated against the pneumococcus attains a high degree of protective power, as shown by animal experiments, against an otherwise lethal dose of the pneumococcus with which the horse was inoculated. The immune serum thus obtained is highly specific and protects only against an organism of the same type as that used in the inoculation. Thus far immune horse-serum with protective power against Type I pneumococcus is the only antipneumococcus serum

which has been found to be of curative value in pneumonia in the human subject.

I have often been impressed with the more favorable aspect of the patients' general condition and the apparent limitation of the spread of the disease after the administration of the serum, but so variable is the course of lobar pneumonia that it is difficult not to be misled in the judgment regarding these matters, and to say in individual cases that similar improvement might not have occurred independently of the serum. The appearance of protective bodies in the patient's blood after the administration of serum is probably due to those contained in the injected material, and can hardly be regarded as evidence of an immunity response on the part of the patient.

The prevention of further invasion of the blood-stream and the consequent checking of the septicemia is strong evidence of curative action in the serum, inasmuch as invasion of the blood by the pneumococcus probably plays an important part in the fatal outcome in pneumonia.

The diminution in mortality is the most significant evidence. The most reliable statistics are those of the Rockefeller Hospital. The mortality in Type I pneumonia without serum is estimated at 25 per cent. Of 107 cases of Type I lobar pneumonia treated with Type I serum at the Rockefeller Hospital, only 8 died—a mortality of 7.5 per cent. There is, however, an element of uncertainty in conclusions drawn from so small a number of cases. Wholly reliable conclusions also cannot be drawn from the comparison of a series of treated cases with an antecedent series of untreated cases. The results are, however, so striking that we cannot disregard them, though they would be more convincing if an equal number of cases of Type I pneumonia could have been reserved as a simultaneous control. Experimental confirmation of the curative value of the serum in Type I pneumonia in monkeys against an otherwise lethal dose of Type I pneumococcus has been obtained by Cecil and Blake, and there can be no doubt of its efficiency.

I am myself convinced of the value of the serum, and think that there is no escape from the obligation to use it in Type I

pneumonia. What precautions should be observed in the use of the serum?

STUDENT: To guard against anaphylaxis.

DR. LORD: How?

STUDENT: By inquiry concerning a previous history of asthma, hay-fever, susceptibility to emanations from horses, or the administration of horse-serum for diphtheria, meningitis, tetanus, or other diseases.

DR. LORD: The unguarded administration of horse-serum to patients with asthma is attended by considerable danger. Eight instances of sudden death and one of collapse have been reported to me by physicians following the administration of antidiphtheria serum to patients with asthma. Many more cases have occurred than have found their way into the literature. Boughton (Jour. Amer. Med. Assoc., Dec. 27, 1919) reports the case of a man subject to attacks of bronchial asthma when in proximity to horses, to whom 1 minim of normal horse-serum was administered intravenously. Within two minutes a typical attack of asthma developed and death followed in forty-five minutes after the injection. Autopsy showed no other significant changes than those found in experimental anaphylaxis. There is still another group which should be mentioned. Patients who have already been treated with antipneumococcic serum and are beyond the refractory stage may pass into a subsequent period of increased susceptibility. Avery, Chickering, Cole, and Dochez (Acute Lobar Pneumonia, Prevention and Serum Treatment, Monographs of the Rockefeller Institute for Medical Research, No. 7, October 16, 1917) refer to an instance of severe anaphylaxis in a patient who had received an intravenous dose ten days before. There is one instance recorded (Cecil, New York Med. Jour., 1918, cvii, 1003) in which the second dose of antipneumococcus serum was given after two weeks during a relapse of the pneumonia, and the patient died. There is no history in this patient of asthma, hay-fever, susceptibility to emanations from horses, or the previous use of horse-serum. It is especially important to emphasize the possible danger in the administration of horse-serum for pneu-

monia, because the intravenous use of alien serum is attended by somewhat greater risk than in its usual subcutaneous injection for diphtheria. We should not, however, be deterred by these considerations. The danger is slight and can be almost wholly excluded by certain precautions. The sensitiveness of the patient should be tested by the observation for one hour of the injection of a small amount of horse-serum *into* the skin. For this purpose it is convenient to have a few cubic centimeters of sterile horse-serum in a small bottle to avoid the opening of a large lot of serum and using a fine needle to inject into the skin 0.02 c.c. of this diluted serum (diluted 1:10 with salt solution), also injecting at the same time into another region an equal amount of sterile salt solution as a control. If the patient is sensitive, usually within a few minutes, an urticarial wheal, surrounded by an area of erythema, appears at the site of the injected serum, the control remaining negative. The intradermal test was negative in this patient and there is thus no contraindication to the administration of serum. Even if no reaction follows the intradermal cutaneous test, it should be an invariable rule to inject a subcutaneous dose of  $\frac{1}{2}$  to 1 c.c. of horse-serum for the purpose of desensitizing the patient and avoiding any possible danger. A desensitizing dose was thus given this patient at 6 P. M. October 11th.

The mortality in pneumonia at this patient's age cannot be definitely stated, but is probably not far from 60 per cent. His appearance is rather ominous, and the outlook with his double pneumonia is probably fully as bad as the average for persons of his age. Extreme youth may be a deterring factor in the use of serum from the difficulty of carrying out the intravenous therapy without nervous exhaustion of the patient or the use of an anesthetic, but this patient's sixty-four years need not deter us. There is, however, a consideration regarding the stage of the disease which merits some comment. It would seem to be the fourth day of the illness. As you will see from his chart, the temperature has been slowly climbing during the past forty-eight hours, and is now at 103.2° F. It is desirable to appreciate that in the application of this as of all forms of serum therapy,

an important relation obtains between the previous duration of the infection and the effectiveness of immune serum. The sooner the serum is given, the more effective it will be. In pneumococcus infections it has been shown by Cole (Jour. Exp.

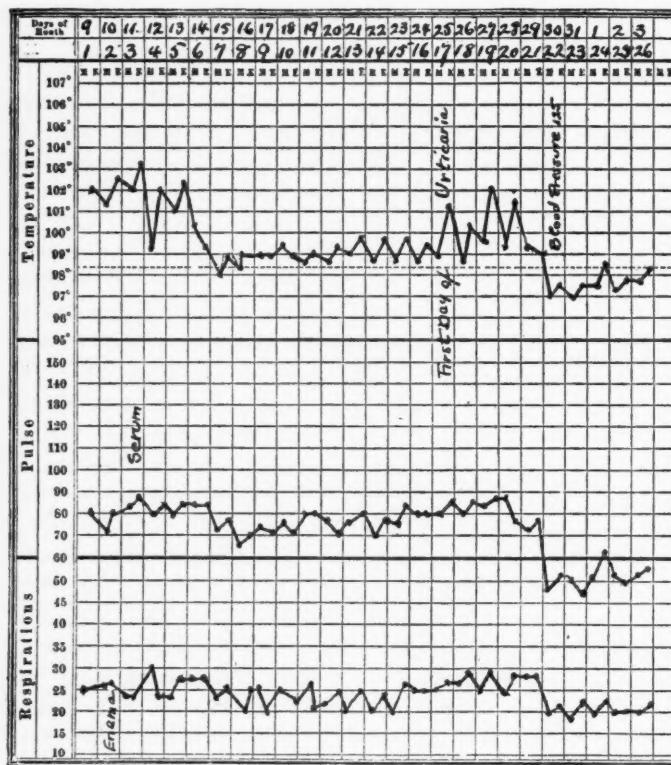


Fig. 187.—Pneumonia.

Med., xxvi, 453, October, 1917) and others that there is an elaboration of soluble inhibiting substances. These substances tend increasingly to diminish the potency of the serum as the disease progresses. A considerable responsibility, therefore,

rests upon you to make the diagnosis of Type I infection at the earliest possible moment, and not to wait until the patient's condition becomes serious and the most opportune time for serum treatment has gone by.

There should be easily accessible laboratories open day and night to which fresh sputum may be sent for the diagnosis of the type of pneumococcus infection. The sputum should be collected in a sterile receptacle from the deeper parts of the respiratory tract. Small amounts of sputum—1 c.c.—suffice for mouse inoculation, but it is important that the specimen come from the involved lung and not from the mouth. It is usually possible to determine the type within from six to eight or ten hours of the time it is received in the laboratory. If larger amounts—3 to 10 c.c.—can be obtained, an almost immediate diagnosis of the type may be made by the coagulation method described by Krumwiede and Valentine (Jour. Amer. Med. Assoc., February 23, 1918).

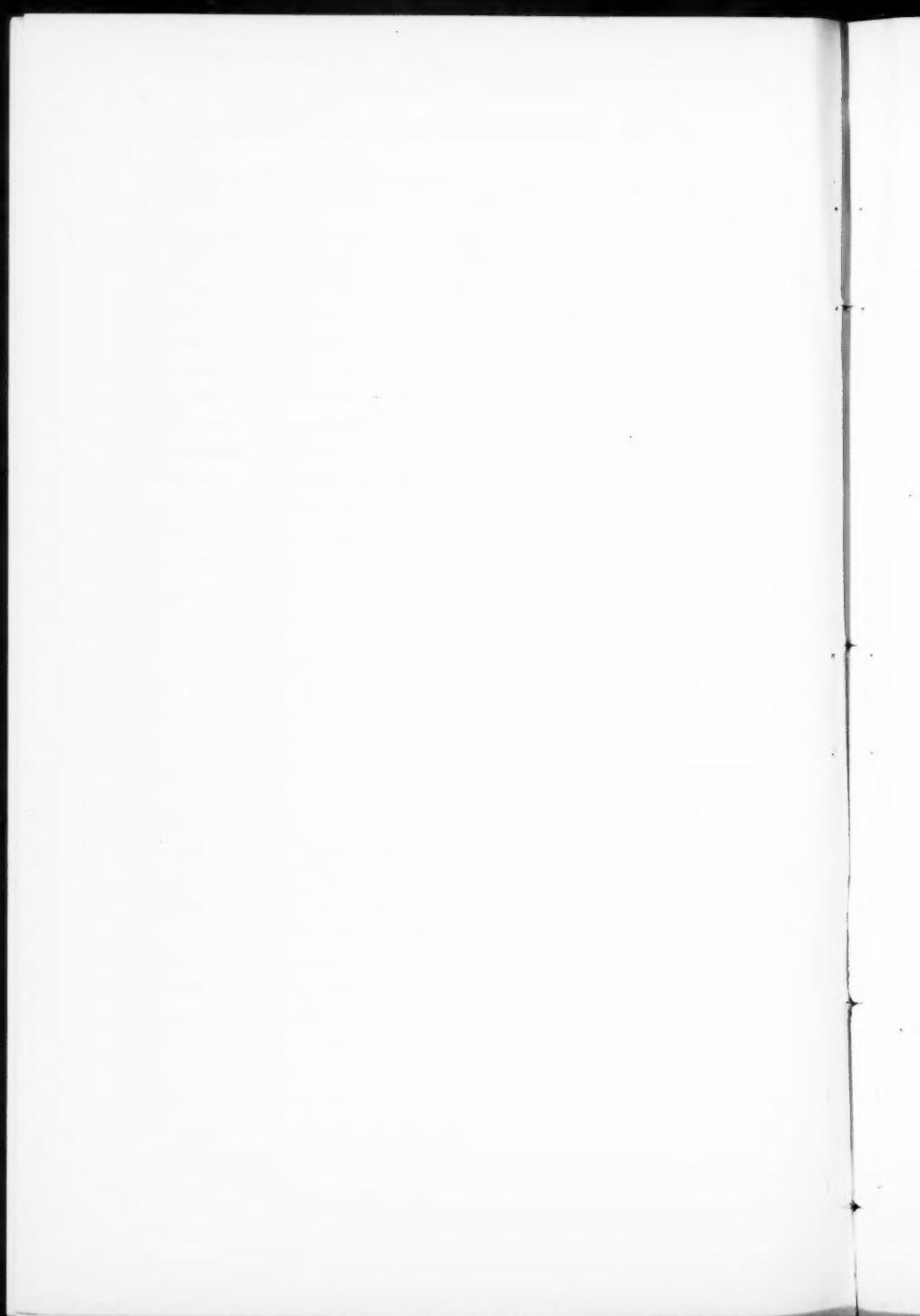
Two hours after the injection of the desensitizing dose of serum in this patient, an injection of 5 c.c. of Type I antipneumococcus serum was given subcutaneously as an added precaution. Two hours later he was given 90 c.c. of the serum intravenously. I have here the apparatus, which you see consists of a three-way stop-cock with attached rubber tubing, one arm of which leads into a 20-c.c. glass syringe, a second into the bottle containing the serum, and the third connects with the needle through which the intravenous injection is made. Dilution of the serum with an equal volume of sterile normal saline solution (freshly distilled) is desirable to maintain freedom of motion of the glass piston of the syringe during the slow injection of the serum. The serum should be at body temperature when given. Adrenalin chlorid (10 minims) and atropin sulphate ( $\frac{1}{100}$  gr.) should be at hand ready for immediate hypodermic use in case symptoms of anaphylaxis occur during the injection. The first 15 c.c. of the serum should be given slowly, fifteen minutes being spent in its administration. The remainder may be given more rapidly. During the injection the onset of an anaphylactic attack may be indicated by symptoms of urticaria, such as tingling

and itching of the skin, scratching or rubbing, and an asthmatic attack with rapid respiration, dyspnea, cough, and cyanosis. Such symptoms warrant the immediate termination of the injection. No symptoms of anaphylaxis occurred in this patient, but one hour after the injection of the serum he had a violent chill, feeble pulse, temperature 105° F. and cyanosis, and his general appearance was rather disturbing. The reaction lasted for about an hour. In the succeeding eight hours his temperature fell to 99.2° F., as shown on the chart, and during this period he perspired profusely. This is the so-called thermal reaction, and, though discomforting to the patient and disturbing to the physician, it is seldom dangerous.

We plan in general to give subsequent doses of serum every eight hours when the temperature, taken every two hours, remains the same or reaches a higher level, to postpone the injection if the temperature is lower than its previous level, comparisons of the temperature being made with that at a corresponding hour in the previous twenty-four hours. But reliance should not be placed entirely on the temperature, and due account should be taken of the patient's general condition and the disposition of the pulmonary process to extend. In this patient the temperature remained for the following two days at a lower level than before. The area of pulmonary involvement in the left lung did not advance. The involvement of the right lower lobe remained practically the same, but there was an extension of the process into the right upper lobe. In spite of the increasing extent of the lung involvement, the pulse remained low and the general condition was strikingly better than before the injection of the serum. In view of the rather severe thermal reaction following the first dose we were thus led to postpone readministration, meanwhile watching his condition from day to day, and, as you see, the temperature fell to normal between the seventh and eighth day. While we cannot be certain in any individual case of the efficiency of the serum, yet the persistence of the temperature at a lower level following the injection and the patient's improved condition in the last few days of his illness, when ordinarily at this period we expect the situation to be more dis-

turbing, suggest that curative action is to be ascribed to the serum.

Fourteen days after the serum was given an urticarial eruption appeared, accompanied by fever, edema of the skin, and joint pains. These symptoms lasted for four days. This complex is spoken of as *serum disease*, and is not infrequent following the administration of alien serum for any purpose. It occurs in about one-half of serum-treated cases in a mild form, giving rise to more severe disturbance in about 10 per cent. An external application composed of carbolic acid  $\frac{1}{2}$  dram, zinc oxid 1 ounce, glycerol 2 drams, and lime-water to make 8 ounces, is most efficient in relieving the pruritus accompanying the urticaria. Adrenalin chlorid subcutaneously in doses of 10 to 15 minimis of a 1 : 1000 dilution is useful at night when the sleep is disturbed by the itching. Readministration of serum after an intermission of more than a few days should be undertaken only with great caution.



## CLINIC OF DR. PAUL DUDLEY WHITE

MASSACHUSETTS GENERAL HOSPITAL

### THE DIAGNOSTIC VALUE OF ELECTROCARDIOGRAPHY OF HEARTS BEATING REGULARLY

THE electrocardiogram is useful in the clinical study of cardiac patients who have a regular pulse as well as in cases of arrhythmia. With this introduction first let me say a few words about the method of study—electrocardiography.

#### THE METHOD

The electrocardiograph is not the first instrument of precision to be adopted in clinical medicine. It follows in the wake of others—the stethoscope, the sphygmomanometer, the x-ray. And yet as one of the newer developments in the theory and practice of medicine it is viewed by some as a mysterious process, which is beyond the possibility even of distant acquaintance in the case of the general practitioner, and the value of which is very doubtful. One sees occasional articles published in the medical journals on the subject of electrocardiography and is inclined to pass them by, especially if they are illustrated by photographic records, the electrocardiograms. The subject does seem at first glance difficult and complicated, but since the electrocardiograph has come to stay, it behooves every doctor sooner or later to learn something about it, if merely to know when or in what cases it would be wise to have such a record taken, the interpretation being left perhaps to the special worker.

Nowadays, in the complete study of an obscure case of heart trouble one does not feel satisfied unless one has used all the methods of diagnosis available. Once upon a time a sketchy history and the palpation of the pulse with or without auscultation

tion of the heart with the naked ear sufficed. Gradually, as various instruments have been invented and their value proved, their use has supplemented the primitive examination of bygone days until one by one the stethoscope, the blood-pressure gage, the *x*-ray, the Wassermann reaction have been accepted as instruments or methods yielding additional information about the heart often valuable and supplementing the more careful history. Now it is the turn of the string galvanometer or electrocardiograph. This instrument also adds its quota of information to that already obtained by other means, and not infrequently this information is of great value. The plea that the apparatus is too costly and technical holds true in the same manner as in the case of the *x*-ray. Every doctor cannot have one, but in every large medical clinic there should be one for consultation.

I shall present now a brief summary of the instrument and of the method of electrocardiography, but for details I recommend that one read Thomas Lewis' little book entitled *Clinical Electrocardiography*. In the middle of the last century it was shown by animal experiments in the laboratory that the heart-beat is attended by a minute electric activity—a current flowing from the base of the heart to the apex. In 1889 it was shown by Waller to be possible to demonstrate the electric activity of the human heart by attaching electrodes to the hands and feet—thus without the necessity of laying bare the heart as had been done in the case of animals. In 1913, at the International Physiological Congress at Groningen, I had the opportunity of seeing Waller repeat his original demonstration. However, the available instrument—the mercury column or capillary electrometer—was too crude for satisfactory records, and there was little progress until in 1903 Einthoven invented the delicate and practicable string galvanometer, which has been given the name of electrocardiograph. Gradually in the years that followed the apparatus and the method were introduced into the clinic, and at last Thomas Lewis put clinical electrocardiography on a firm foundation. Recent years have proved the value of Einthoven's galvanometer and the soundness of Lewis' teachings.

The modern instrument consists of a powerful electromagnet

between the poles of which is a microscopic conducting fiber, which is connected with the electrodes attached to the extremities of the patient. The minute electric waves which precede and attend the actual heart-beats are transmitted from the body to the "string" or fiber between the poles of the electromagnet. The interaction between the magnetic waves of the poles and the magnetism induced by the tiny current in the tiny fiber makes the fiber move. This movement is magnified and



Fig. 188.—B. H. R. Normal. *Regular pulse of 86 per minute.* In this figure and in those that follow abscissæ = 0.2 second and ordinates = 0.1 millivolt (see text); *P* = auricular wave; *R* and *T* = ventricular waves (*R* represents in the figures the entire first ventricular complex *Q-R-S*); 1, 2, and 3 refer to Leads 1, 2, and 3.

projected upon a camera aperture by a bright light and a system of lenses. A moving plate or film in the camera obtains a photographic record of the movement of the string. This record is the electrocardiogram.

The electrocardiogram is made up of three chief deflections or waves, mostly upright, with each heart-beat—*P*, *Q-R-S*, and *T*. These letters were selected by Einthoven because they had no particular significance, which was a wise measure at the time,

since the cause of these individual waves was not clear when they were first observed. Even now the story is not complete, but it is known that *P* stands for the electric impulse in the *auricles*, *Q-R-S*<sup>1</sup> stands for its passage into the *ventricles*, and *T* occurs during *ventricular contraction* (Fig. 188). The time is usually recorded in fifths of a second—by abscissæ in the figure. The ordinates in the figure and in those that follow represent tenths of a thousandth of a volt (tenths of a millivolt) in terms of electromotive force.

In the description of the method there is one other important point and that is with regard to the so-called *leads*. It has been found of value to connect three parts of the body with the galvanometer—the right arm, the left arm, and the left leg. These form a triangle of electric forces. If the right arm and left arm are connected with the string we have *Lead 1*. The right arm and left leg give us *Lead 2*, and the left arm and left leg give *Lead 3*. It has been shown that Leads 1 + 3 equal Lead 2. The axis of Lead 2 is normally parallel or nearly parallel to the long axis of the heart, and so is the record preferred for analysis of arrhythmias and most other abnormalities, because it gives the biggest waves. Leads 1 and 3 are also photographed in routine examination because of certain values which we shall discuss below.

#### CLINICAL FINDINGS

Medical men who are now somewhat acquainted with electrocardiography at once recognize its clinical value in the rapid and easy analysis of the irregular or very rapid or very slow pulse. Sinus arrhythmia, the premature contractions or extrasystoles (whether auricular or ventricular in origin), paroxysmal tachycardia, auricular flutter, auricular fibrillation, and heart-block are terms so heralded of late years that they are reaching the remote regions of medical practice, and even the doctor far from medical centers is becoming aware that these abnormalities of cardiac rhythm exist and have some significance, and that, thanks to the work of Mackenzie and Lewis in particular, can

<sup>1</sup> For convenience I shall refer to the *Q-R-S* complex simply as *R* in the figures and in further discussion.

be readily analyzed by graphic methods even though the doctor himself is not acquainted with these methods. For a concise description of these abnormalities of the pulse one cannot do better than to turn to Lewis' book, *Clinical Disorders of the Heart-beat*.

On the other hand, the medical men are not very numerous who are aware of the value of electrocardiography in the clinical study of heart conditions in cases with a regular pulse, neither excessively slow nor excessively fast—the regular pulse of 50 to 100 per minute. Many a doctor would not dream of the possi-

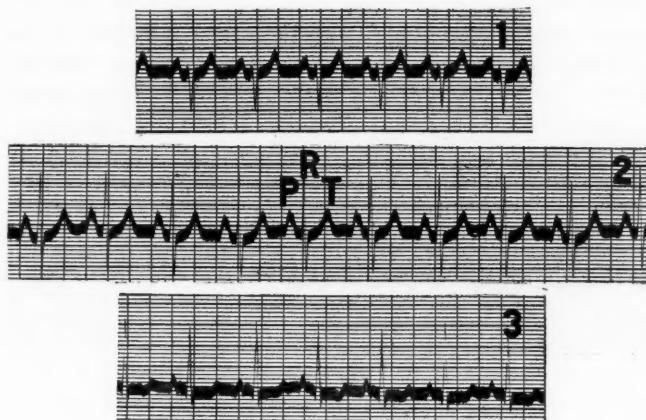


Fig. 189.—M. O. Mitral stenosis. *Regular pulse of 98.*

bility of the electrocardiogram helping in the case of a patient with a regular pulse of 72 to the minute. It is of just such cases that I wish to speak now and to show examples.

I shall take up in detail these various conditions which with a regular pulse of moderate rate show characteristic electrocardiograms, considering the auricular, ventricular, and general conditions in order.

1. **Auricular Hypertrophy.**—This is evidenced by the very high or wide *P* or auricular wave of the electrocardiogram (beyond  $\frac{3}{10}$  millivolt or 3 mm. high, or more than 0.1 second

wide—Fig. 189). It is almost always indicative of the hypertrophy of the auricles found with mitral stenosis, and so may be considered as evidence of mitral stenosis.

**CASE I.—*Mitral Stenosis.***—M. O. Male, fourteen years of age. Schoolboy. Born in Russia. Tonsillitis very often, till tonsillectomy four years ago. Symptoms of palpitation, precordial pain, and dyspnea on slight exertion for past one and a half years. Heart enlarged, especially transversely (x-ray). Marked systolic, diastolic, and presystolic murmurs at the apex. In the electrocardiogram of this patient (Fig. 189) note the tall wide *P* (auricular) deflection in Lead 2. Incidentally, there is a definite abnormal preponderance of the right ventricle, as seen in Leads 1 and 3 (see discussion of ventricular preponderance below). *Observe that this is a regular pulse of 98 to the minute.*

**2. Auricular Flutter.**—Rarely, with a very rapid auricular rate arising from an abnormal (=ectopic) focus in the auricles,

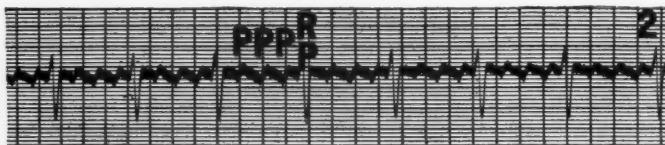


Fig. 190.

there may be such a regular high grade of block that only every fourth or sixth auricular stimulus gets through the auriculoventricular junction to the ventricles. For example, the auricles may be contracting at 300 per minute, and with a 4 to 1 block the ventricles, and so the pulse, would beat at one-quarter of 300, or 75, to the minute with great regularity. Auricular flutter is usually evidence of severe myocardial damage or poisoning, most commonly seen in rheumatic or arteriosclerotic hearts, while the high-grade block means the effect of digitalis (usually) or insufficiency of the path of auriculoventricular conduction from other cause. In the electrocardiogram the rapid auricular deflections, *P-P*, are clearly seen and at intervals the normal ventricular complexes, *R-R* (Fig. 190).

**CASE II.—Auricular Flutter. Myocarditis (? Cause).**—W. S. Male. Thirty-seven years old. School-teacher. Born in Massachusetts. Typhoid fever at eighteen years of age, followed by weakness in legs, especially the right, ever since. Symptoms of dyspnea and weakness on exertion for several years past. Heart large by x-ray<sup>1</sup> (transverse diameter of 18 cm.), with apex in the sixth space. Auscultation showed a rapid, slightly irregular action without murmurs. Wassermann reaction negative. Urine normal. Electrocardiogram showed auricular flutter, with rapid, slightly irregular ventricular response. Digitalis was begun at once, and in one week after 2.4 grams of digitalis leaves 4 to 1 heart-block was found (Fig. 190), the auricles *P-P* beating regularly at 244, and the *ventricles (R-R)* beating *regularly and quietly* at 61.



Fig. 191.

**3. Ectopic Auricular Rhythm.**—This means a cardiac action resulting from the production of stimuli at an abnormal point in the auricle, and is evidence of abnormal irritability of the auricular myocardium or of abnormal depression of the sino-auricular node. Auricular flutter and paroxysmal tachycardia are the more usual and more severe examples of this rhythm, but rarely one may find the condition with a relatively slow pulse-rate. In the electrocardiogram the ectopic auricular impulse is usually evidenced by a flat or inverted *P* (Fig. 191).

**CASE III.—Ectopic Auricular Rhythm. Aortic Regurgitation. Myocarditis, Chronic.**—E. B. Male, fifty-three years old. Stonemason. Born in Italy. Past history negative. Symptoms of dyspnea on exertion for past ten months. Wassermann

<sup>1</sup> All x-ray measurements given in this and in the later cases are those made with the patient 7 feet from the tube.

reaction negative. *x*-Ray showed a very large heart—18.7 cm. transversely; great vessels 7 cm. wide. Auscultation and blood-pressure showed presence of aortic regurgitation. Died one year later. Electrocardiogram (Fig. 191) at time of hospital examination noted above showed inverted *P* waves, but a *regular pulse of 54 to the minute*.

**4. Auriculoventricular Rhythm (= Atrioventricular Rhythm).**—This means a heart action arising from stimulus production in the junctional tissues between auricles and ventricles, so that auricles and ventricles beat simultaneously. It is a very rare condition, and signifies either a paralysis of the normal pacemaker in the sino-auricular node, or else an irritation of the junctional tissues. It is not of much importance clinically. In the electrocardiogram (Fig. 190) the *R* (ventricular) and *P* (auricular) waves fall together or very close together, the *P* wave inverted.

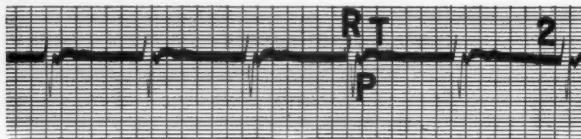


Fig. 192.

Under this same heading may be added the very rare cases of auricular standstill in which the ventricle continues to beat from the junctional tissue pacemaker, but in which the auricle is completely paralyzed (Fig. 191). Finally, we have also the condition of ventricular escape in which an irritable ventricle beats regularly, but more rapidly than the auricle (Fig. 194). Both of these conditions—auricular standstill and ventricular escape—are dependent on the activity of the junctional tissue pacemaker and are apt to result from digitalization.

**CASE IV.—Auriculoventricular Rhythm (= Atrioventricular Rhythm). Myocarditis (? Cause).**—W. S. Described above under "auricular flutter." Following his flutter, fibrillation of the auricles was induced by digitalis. The drug was stopped

and the heart after four days became regular, with no evidence of auricular action. Finally, one week after the disappearance of auricular fibrillation and all evidence of auricular action, the auricular wave (*P*) reappeared, inverted, in the electrocardiogram immediately following the ventricular complex (*R*) (Fig. 192). Here the impulse arises in the junctional tissue and travels in both directions, reaching and stimulating the ventricles before the auricles.<sup>1</sup> Observe that the *pulse is perfectly regular at 46*.

CASE V.—*Auricular Standstill. Cardiosclerosis + Digitalis.*—W. J. B. Male, sixty-nine years old. Musician. Born in New York. Past history negative. Symptoms of precordial pain and dyspnea began two years ago; recently cough and edema of legs developed also. *x*-Ray showed an enlarged heart, transverse diameter of 16.3 cm., cardiac apex in sixth space. Slight to moderate hypertension. Arteriosclerosis. Wassermann re-



Fig. 193.

action negative. Radial pulse tracing showed occasional ventricular premature beats followed by alternation. Patient died less than fifteen months later. Electrocardiogram (Fig. 193) showed no evidence of auricular action in any lead after the administration of digitalis leaf, 6 grams in the course of two weeks. Also there was constant electrocardiographic evidence of defective intraventricular conduction of the right bundle-branch block type. *The pulse was regular at 80 per minute.*

CASE VI.—*Ventricular Escape. Luetic Myocarditis + Digitalis.*—E. J. Y. Male, fifty-six years old. Laborer. Born in New Brunswick. Chancre at age of thirty-three. Symptoms of myocardial weakness for past six or eight weeks. Wassermann reaction strongly positive. *x*-Ray showed a big heart, 18.8 cm. in transverse diameter, with apex in sixth space, and a

<sup>1</sup> This case was described in detail in the Archives of Internal Medicine, October, 1915, xvi, 517.

wide aortic arch—diameter of great vessels 9.7 cm. Luetic aortitis. Pulsus alternans by radial pulse tracing. Patient received 1.8 grams of digitalis leaves in nine days. Electrocardiograms showed auricular standstill three days after stopping the drug and ventricular escape four days later (Fig. 194). In this record one notes that the ventricular wave *R* appears twice as frequently as the auricular wave *P*. *The pulse was regular at 80 per minute.*

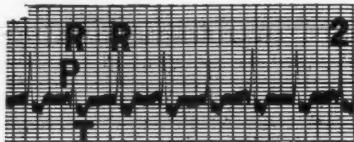


Fig. 194.

**5. Auriculoventricular Heart-block.**—This may be of three grades. It is not rare.

(a) Simple delay in auriculoventricular conduction, without any dropped beats. This means either depression of the conducting mechanism by digitalis or other toxin, or else definite pathologic alteration of the node or bundle between auricles and ventricles. The commonest cause is digitalization, but if one

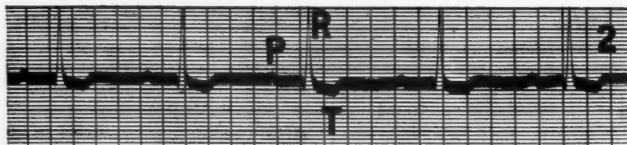


Fig. 195.

rules out digitalis, the condition should be considered as serious ordinarily. Moreover, it is known that digitalis readily induces the condition in damaged or weakened tissue. In the electrocardiogram one finds a time interval between *P* (auricular) and *R* (ventricular) waves of over 0.18 second (Fig. 195).

**CASE VII.—Delayed Auriculoventricular Conduction. Luetic Myocarditis and Cardiosclerosis.**—T. C. Male, seventy-two years old. Harness maker. Born on the Isle-of-Man. Chancre

at age of twenty-two years. Symptoms of dyspnea and precordial pain on exertion for the past four months. Wassermann reaction positive. *x*-Ray showed some enlargement of the heart—13.6 cm. transverse diameter, and slight increase in width of great vessels, 7 cm. Auscultation and blood-pressure showed marked aortic regurgitation. General arteriosclerosis. Prior to the electrocardiogram patient was thought to have had little if any digitalis; the record (Fig. 195) shows a long *P*-*R* interval (about 0.3 second) and an inverted *T* wave, both of which conditions suggest digitalization. His bad heart alone might conceivably account for this condition. *His pulse was regular at 55.*

(b) *Two-to-one Auriculoventricular Heart-block*.—Here every second auricular impulse (*P*) fails to produce a ventricular response (Fig. 196). For example, with an auricular rate of 100,



Fig. 196.

the ventricles would beat at 50 per minute, both perfectly regular. It is a more serious condition than simple delay in conduction.

CASE VIII.—*Two-to-one Auriculoventricular Heart-block. Myocarditis (? Cause)*.—A. B. B. Female, six years old. Born in Massachusetts. Infantile paralysis at age of four months, with involvement of left arm. Tonsils and hypertrophied left cervical glands removed two years ago; heart apparently normal then. Bradycardia for past six months. No other symptoms or signs. Heart does not appear abnormal except for usually slow pulse, always regular, varying in rate from 52 to 72 per minute. Electrocardiogram (Fig. 196) showed 2 to 1 auriculoventricular heart-block with a *regular ventricular rate of 53 per minute*.

(c) *Complete Auriculoventricular Heart-block*.—This is the

highest grade of all, in which there is no longer any association between auricles (*P*) and ventricles (*R*), but with a regular ventricular action and pulse (Fig. 197). Rarely this idioventricular rate may be relatively high, at 50 or more to the minute, apparently the result of an irritable ventricular pacemaker or one situated high in the junctional tissues where the automatic rates are relatively rapid. Complete heart-block is a serious condition meaning wide-spread myocardial damage.



Fig. 197.

**CASE IX.—*Complete Heart-block. Myocarditis* (? *Diphtheritic*).**—C. E. A. Female, twenty-four years old. Violin teacher. Born in Massachusetts. Never strong; always easily tired. Very sick in infancy with measles, *diphtheria*, and scarlet fever. Heart irregular at twelve years of age. Symptoms of dyspnea, precordial pain, and exhaustion on moderate exertion for past eight years. *x*-Ray showed a large heart—13.3 cm. in transverse



Fig. 198.

diameter, with a normally sized aortic arch. Apex impulse in the fifth space. Blowing systolic murmur heard over precordia, loudest at apex. Pulse-rate regular, varying between 52 and 65. Electrocardiogram (Fig. 197) showed an auricular rate of 96 per minute and a *regular ventricular rate of 65*.

**CASE X.—*Complete Heart-block. Cardiosclerosis*.**—J. R. H. Male, sixty-nine years old. Attendant officer. Born in Massachusetts. Scarlet fever at six years of age. Otherwise past

history negative. Symptoms of weakness, dyspnea, and biliary colic for past three or four months. Wassermann reaction strongly positive. x-Ray showed cardiac enlargement, 18.4 cm. transverse diameter; aortic arch 6.9 cm. wide. Electrocardiogram (Fig. 198) shows complete dissociation of auricular (*P*) and ventricular (*R*) waves. The auricular rate was 97 per minute. *The pulse was regular at 51 to the minute.*

**6. Intraventricular Heart-block.**—By the term "auriculoventricular block" we mean blocking of the impulse between

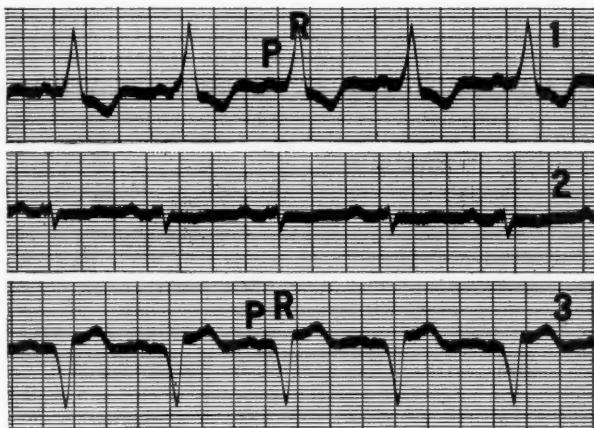


Fig. 199.

auricles and ventricles; by "intraventricular block" we mean trouble further down on the ventricular side of the junction, specifically below the split of the bundle of His into its branches. This may be of various grades and types also, and is always significant of considerable myocardial damage or poisoning. It is more important evidence of serious heart trouble than auriculoventricular block itself, with the possible exception of complete heart-block. Yet in these cases particularly we usually find a regular pulse of normal rate. The association of this condition so often with angina pectoris should make the electrocardiogram

of use in the study of doubtful cases of angina. Intraventricular block is not infrequent. It is of three types, as follows:

(a) "*Right Bundle-branch Block.*"—This results from lesion of the right main branch of the auriculoventricular bundle of His, which branch conducts the cardiac impulse to the right ventricle from the junctional tissues, where the impulse is received from the auricles. The defect is usually permanent and evidence of very serious myocardial disease, but it may be temporary or toxic. In these cases the left ventricle beats first, the impulse reaching the right ventricle directly through the muscular continuity of the two ventricles. In the electrocardiogram Leads 1 and 3 are the necessary leads for detecting this condition. If in Lead 1 we find an upright *Q-R-S* complex more than 0.1 second in duration and in Lead 3 an inverted *Q-R-S* complex more than 0.1 second in duration, we conclude that right bundle-branch block is present (Fig. 199).

CASE XI.—*Right Bundle-branch Block. Cardiosclerosis.*—A. L. Male, fifty-seven years old. Russian pedler. Symptoms of dyspnea and weakness on slight to moderate exertion for years. Heart enlarged, with apex impulse in sixth interspace, but without murmurs. Nephritis with marked hypertension. Glycosuria. General *arteriosclerosis*. Cardiac failure. Graphic records showed at times pulsus alternans, ventricular premature contractions, and paroxysmal auricular fibrillation. Patient died in December, 1916. Electrocardiograms in 1915 and 1916 always showed block in the right bundle-branch (Fig. 199). *The pulse was regular at rate of 86.*

(b) "*Left Bundle-branch Block.*"—This is a much rarer condition, about one-tenth as common as the right-branch block. The left branch is wider and larger than the right and so is not so apt to be interrupted by lesions. It may be that it is correspondingly more serious when found. To detect left bundle-branch block the electrocardiogram is essential. Lead 1 shows an *inverted Q-R-S* complex more than 0.1 second in duration, while Lead 3 shows an *upright* complex more than 0.1 second wide (Fig. 200).

CASE XII.—*Left Bundle-branch Block. Cardiosclerosis.*—

W. G. Male, forty-nine years old. Russian tailor. Past history negative except for alcohol, 5 or 6 whiskies daily for past six or seven years. Symptoms of dyspnea on exertion for past few years, worse during last nine months, with onset of abdominal pain, orthopnea, edema, and weakness. Heart enlarged with weak first sound and double second sound at apex, without murmurs. Liver enlarged. Ascites. Hydrothorax. Edema of feet and legs. Wassermann reaction negative. Electrocardiogram (Fig. 200) showed marked aberration of the ventricular waves (*R*). *The pulse was regular at rate of 71.*

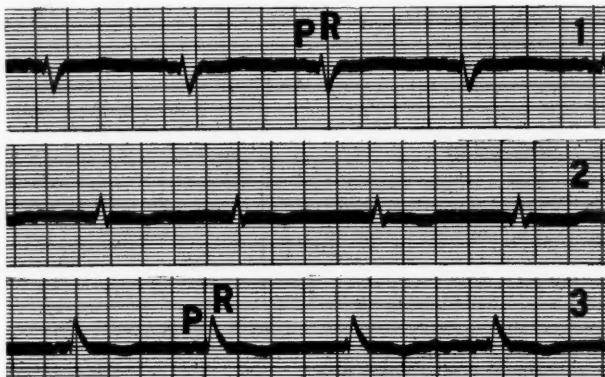


Fig. 200.

(c) *Arborization Block*.—The main branches of the auriculoventricular bundle of His spread out quickly under the endocardium of the ventricles into a perfect network of branches. It is quite natural to expect to find frequent evidence of defect in impulse conduction through this arborization. More and more cases are coming to light in which one sees evidence of such disturbance—in fact, at the present moment every little notch or hesitation of the ventricular wave of the electrocardiogram, even in Lead 3, is being considered by some as evidence of arborization block. This is too extreme, for one may see notching of the *Q-R-S* complex normally in Lead 3. But, speaking conserva-

tively, one sees numerous cases in which though there is no clear-cut right or left bundle-branch block, there is much evidence of abnormal impulse distribution in the ventricles. It is to such cases that we may apply the term "arborization block." We should look particularly in Lead 2 of the electrocardiogram for this condition, shown by clear notching or increased duration

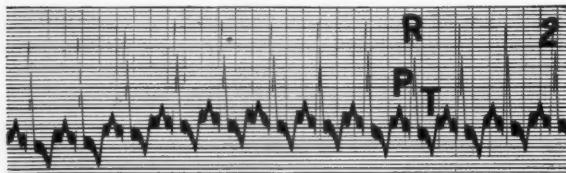


Fig. 201.

(width) of the *Q-R-S* complex beyond the normal limit of 0.1 second. When definite arborization block is found it is a sign almost as serious as the bundle-branch type (Fig. 201). Rarely one may find an alternation in height or shape of the *R* waves, already too wide. This is probably as significant as pulsus alternans. It signifies variation in the capacity of a weakened intraventricular conduction system (Fig. 202).

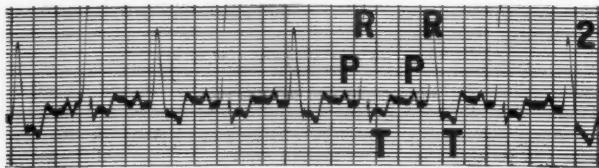


Fig. 202.

**CASE XIII.—Arborization Block. Rheumatic Heart Disease.**

—H. P. Male, twenty years old. Born in Massachusetts. Rheumatic fever at ten years of age and every year since. Symptoms of dyspnea for past eight years, and palpitation and weakness now. Heart very large, with soft, blowing systolic murmur over precordia, loudest at the apex. Fingers markedly

clubbed and cyanotic. Radial pulse tracing showed frequent ventricular premature beats followed by marked pulsus alternans. Patient died within two years. Electrocardiogram (Fig. 201) showed a high split *R* wave of slightly increased duration, and a markedly inverted *T* wave in Lead 2. Patient had not been having digitalis for two weeks prior to electrocardiogram. *The pulse was regular at rate of 106.*

**CASE XIV.—Alternation of Electrocardiogram. Aortic Stenosis and Regurgitation.**—L. A. B. Male, twenty-eight years old. Jewelry shipper. Born in Massachusetts. Past history negative. Symptoms of dyspnea on moderate exertion for one year and substernal pain and weakness for the past six months. *x*-Ray showed an enlarged heart, 16.6 cm. transverse diameter, with great vessels 8 cm. wide. Very rough systolic murmur at base, loudest in aortic area; diastolic murmur lower pitched, heard along left border of sternum. Wassermann reaction negative. Died ten weeks later. Electrocardiogram (Fig. 202) showed marked alternation of the ventricular waves (*R*) with some increase in duration of these ventricular complexes beyond the normal. *The pulse was regular at 98.*

**7. Ventricular Preponderance.**—Relative increase in muscle mass of one or the other ventricle. One of the findings of the electrocardiogram is that of abnormal preponderance of either ventricle. It is sometimes useful to know whether the heart shows right or left ventricular preponderance in doubtful cases, as with an obscure loud systolic murmur at the base where pulmonic and aortic stenosis are under consideration as possible causes. Here the first and third leads give the necessary information.

(a) *Left Ventricular Preponderance.*—If the *Q-R-S* complex in Lead 1 is very positive and in Lead 3 very negative, we may conclude that there is definite abnormal preponderance of the left ventricle.<sup>1</sup> Practically, one may add the height of the upward

<sup>1</sup> In such cases the duration (width) of the ventricular complexes must be within normal limits. Otherwise the condition is masked by intraventricular block of the bundle-branch type.

excursion in Lead 1 in millimeters to the depth of the downward excursion in Lead 3, and then subtract the sum of the downward excursion in Lead 1 and the upward excursion in Lead 3.<sup>1</sup> If the result lies between +20 and +30, we have evidence of doubtful or slightly abnormal preponderance of the left ventricle. If the result is more than +30, we may be sure that there is abnormal left ventricular preponderance (Fig. 203). This is most commonly seen in cases of aortic regurgitation or of chronic hypertension, and is of fairly frequent occurrence.

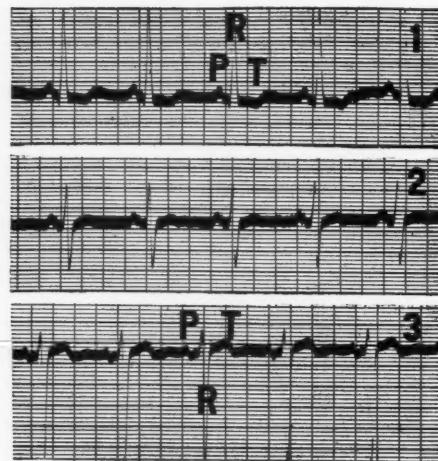


Fig. 203.

**CASE XV.—Left Ventricular Preponderance. Aortic Regurgitation.**—G. C. Female, sixty-nine years old. Housewife. Born in Italy. Symptoms of increasing dyspnea and precordial pain on exertion for past sixteen years. Heart much enlarged, with apex in sixth space and dilated aortic arch. Auscultation and blood-pressure (230 mm. systolic, 85 mm.

<sup>1</sup> Carter, E. P., and Greene, C. H., have recently published further observations on The Electrocardiogram and Ventricular Preponderance (Arch. Int. Med., 1919, xxiv, 638) which indicate that the easily determined inclination of the axis of the heart may serve as a more reliable "quantitative guide to cardiac change" than the index described above.

diastolic) showed presence of aortic regurgitation. Wassermann reaction negative. Radial pulse tracing showed pulsus alternans. Electrocardiogram (Fig. 203) showed marked left ventricular preponderance (index of +46). *The pulse was regular at rate of 78.*

(b) *Right Ventricular Preponderance.*—The electrocardiographic findings of left ventricular preponderance are reversed in this condition. A deep downward excursion in Lead 1 with a high upward excursion in Lead 3 gives us evidence of right ventricular preponderance. Using the same procedure as mentioned

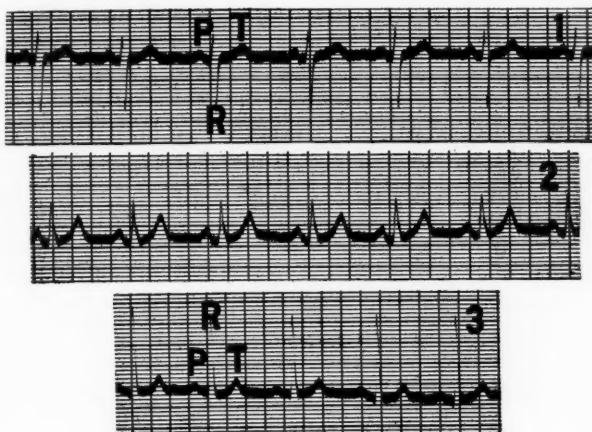


Fig. 204.

before, if we find an index between —15 and —18 we suspect abnormal preponderance of the right ventricle, while figures more negative than —18 always mean abnormal right ventricular preponderance (Fig. 204). This is most commonly seen in marked mitral stenosis and congenital heart disease, rarely in chronic emphysema.

**CASE XVI.—Right Ventricular Preponderance. Congenital Heart Disease (Pulmonary Stenosis).**—C. M. Female, twenty-seven years old. Housewife. Born in Roumania. Past history negative except for one miscarriage; one child living and well.

Symptoms of palpitation for ten years, and dizziness and dyspnea for two years past. Steadily losing ground. Heart showed marked systolic murmur and thrill at base, especially pronounced in pulmonic area. Electrocardiogram (Fig. 204) showed marked preponderance of the right ventricle (index of -25). *The pulse was regular at rate of 68.*

8. **Dextrocardia.**—With inversion of all the waves, *P, Q-R-S, and T* in Lead 1, with little change in Leads 2 and 3, one may make a certain diagnosis of congenital dextrocardia (Fig. 205). If the heart is pushed or pulled over to the right by some patho-



Fig. 205.

logic process, one does not obtain this picture. Hence, given a case of dextrocardia, the electrocardiogram aids one in determining whether it is congenital or acquired.

**CASE XVII.—*Dextrocardia, Congenital.***—N. M. C. Female, thirty-five years old. Housewife. No cardiac symptoms; entered hospital for acute salpingitis. Heart examination showed the apex in the fifth right interspace with right border 9 to 10 cm. to the right of midsternum; left border 5 cm. to left of midsternum. The electrocardiogram (Fig. 205) showed complete inversion of Lead 1. *The pulse was regular at rate of 96.*

**9. Myocardial Weakness.**—Not infrequently one finds electrocardiographic evidence of a very weak myocardium in cases with a regular pulse. This is shown by one or both of two findings: a very low or flat *T* wave (when one can rule out digitalis effect) and small excursion of all waves in all leads (both findings shown well in Fig. 206).

**CASE XVIII.—*Myocardial Weakness. Arteriosclerosis.***—J. F. M. Male, sixty-three years old. Born in Maine. Symptoms of dyspnea, precordial pain, weakness, edema, and blurring of vision for past three months. Wassermann reaction negative.

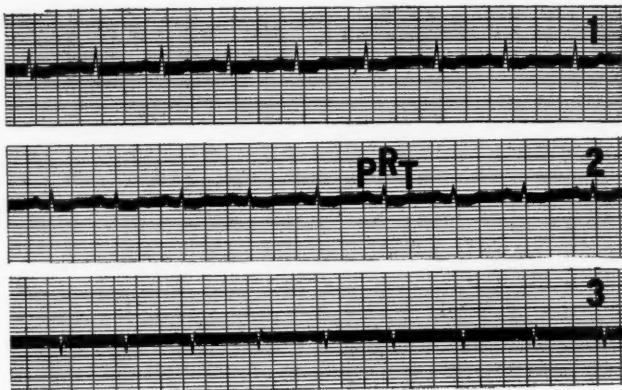


Fig. 206.

Hypertension. Retinitis. Cardiac failure. Died twelve days after electrocardiogram was taken. Postmortem examination showed arteriosclerosis generalized, including kidneys and heart, and lymphangio-endothelioma of retroperitoneal region, extending into the inferior vena cava and hepatic veins, with thrombi in inferior vena cava, hepatic, iliac and renal veins, and right auricle. Electrocardiogram (Fig. 206) showed very small diphasic *T* waves, and very small excursion of all waves in all leads. *The pulse was regular at rate of 102.*

**10. Digitalis Effect.**—It has been discovered in recent years that digitalis will ordinarily flatten and invert the *T* wave of the

electrocardiogram which in Lead 2 is normally upright (Fig. 207). Full confirmation of this fact has given another incentive to the routine study of hearts by electrocardiography. Slight, moderate, or marked digitalization of a heart may be determined and followed by the electrocardiogram. This change in shape of the *T* may be seen in digitalization long before a slowing of the pulse or the production of heart-block, or the finding of a coupled or bigeminal pulse. The pulse may be regular at 72 to the minute.

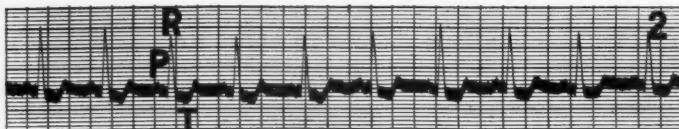


Fig. 207.

**CASE XIX.—Digitalis Effect. Inversion of *T* Wave.**—L. L. Female, fifty-three years old. Housewife. Born in Massachusetts. Luetic myocarditis and aortitis with aortic regurgitation. Symptoms of substernal pain and dyspnea off and on for several years, worse on exertion and of late. *x*-Ray showed enlarged heart, 14 cm. in transverse diameter; great vessels 6.4 cm. wide. Cardiac apex in sixth space. Auscultation and blood-pressure

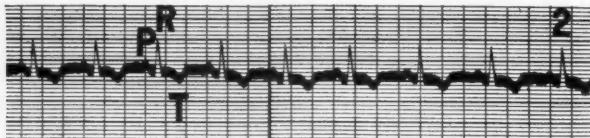


Fig. 208.

showed presence of aortic regurgitation. Wassermann reaction strongly positive. The electrocardiogram (Fig. 207) showed inversion of the *T* wave after 2 grams of digitalis leaf in one week. *The pulse was regular at rate of 96.*

**11. Hypothyroidism.**—Another condition which carries with it ordinarily a low or flat or inverted *T* wave is hypothyroidism (Fig. 208). Myxedema and cretinism act similarly. With im-

provement after feeding thyroid gland, the *T* wave tends to become more positive.

CASE XX.—*Cretinism*.—H. L. Female, twenty years old. Born in Maine. Very thin till eight years old, since that time "fat." Stopped growing at about ten years of age. Physical examination showed typical cretinism. Heart apparently normal. Basal metabolism was —17 per cent. (below normal) before treatment and +20 per cent. (above normal) after two months of thyroid gland therapy. The electrocardiogram (Fig. 208) showed a definitely inverted *T* wave before thyroid

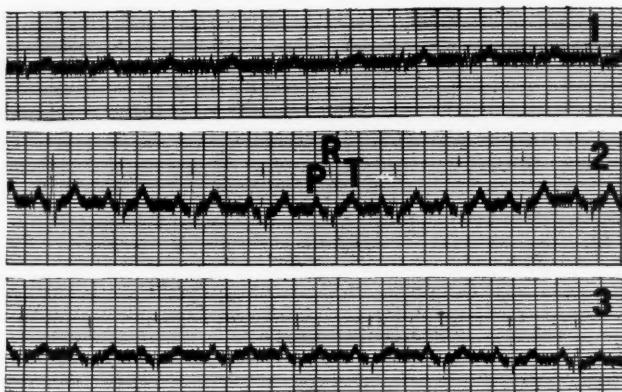


Fig. 209.

administration, and a definitely positive *T* wave after two months of treatment. *The pulse was regular at rate of 98.*

12. **Tremor**.—Finally, one often sees in the electrocardiograms of nervous people, and more often in cases of hyperthyroidism or Graves' disease, an irregular fine oscillation due to the general body tremor (Fig. 209). This occurs most frequently with tachycardia.

CASE XXI.—*Tremor. Neurosis*.—J. E. K. Male, thirty-two years old. Foreman in factory. Born in Massachusetts. Always nervous, but much worse since mental strain due to

sickness in family one year ago. Heart normal except for tachycardia. Tremor. No definite evidence of hyperthyroidism. The electrocardiogram (Fig. 209) showed normal rhythm, the regular cardiac waves somewhat obscured by a marked tremor of the "string" in every lead. *The pulse was regular at rate of 98.*

#### SUMMARY

In the study of heart conditions, when the pulse is regular and even at a perfectly normal rate, the electrocardiogram is sometimes very useful.

The employment of the second lead alone will show many things. It may reveal an auriculoventricular heart-block of simple delay in conduction without dropped beats, a two-to-one block, or a complete block with a relatively high ventricular rate. It also may show arborization block or alternation, or the frequent flat or inverted *T* of digitalization, of a weak myocardium, or of hypothyroidism. It may reveal the auricular hypertrophy of mitral stenosis, or an unrecognized auricular flutter or ectopic auricular rhythm, or an auriculoventricular junctional rhythm. Finally, it may give evidence of a marked tremor so often found in exophthalmic goiter. In every case the pulse-rate may be perfectly regular and usually not far from the normal average in rate.

The use of the first and third leads alone may reveal marked intraventricular (bundle-branch) heart-block so serious in significance, or abnormal preponderance of one or the other ventricle.

The use of the first lead alone may reveal the presence of congenital dextrocardia.

Very small deflections in all leads indicate usually a very weak myocardium.

## CLINIC OF DR. ROGER I. LEE

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### ALBUMINURIA IN YOUNG MEN

We doctors are so accustomed to deal with sick people that we have built up all of our standards and tests from the accumulated data of sick people rather than from well people. This has been particularly brought home to us when we examine any large group of presumably well individuals. The examination for life insurance, the routine physical examination of any group of individuals, and, more recently, the examination for the army, has caused a considerable modification of the usually accepted standards of health and disease.

The particular standard which I have in mind is the test for albumin in the urine. Albuminuria has been hitherto recognized as perhaps the most common symptom of kidney damage. It has been adequately noted that albuminuria does appear in fever, in which it is supposed that the kidney undergoes a cloudy swelling. Perhaps more recently it has been granted that albuminuria may occur as a result of severe physical exertion. The literature contains, furthermore, a goodly number of isolated cases of what is usually called albuminuria of adolescence, or physiologic albuminuria, or orthostatic albuminuria. Such an albuminuria has been reported in the past as of somewhat unusual occurrence, and noteworthy because it accompanied none of the usual symptoms or signs of kidney damage.

Several years ago, when making, as a routine, the complete physical examination of the entire freshman class at Harvard University, I was able to point out that 1 out of 20 of these young men, or 5 per cent., presented albuminuria in a single specimen of urine, passed at the time of examination. The actual per-

centage of Bright's disease was, however, only about  $\frac{1}{10}$  of 1 per cent. Since that time I have repeated these observations, so that I now have observations on approximately 5000 young men, between the ages of sixteen and twenty-four, and the percentage still holds good; namely, that 5 per cent. of these young men, on a routine physical examination, will show albuminuria in a single specimen passed at the time of the examination. By "albuminuria" I do not mean the amount usually designated as the "slightest possible trace," but a very definite ring, when nitric acid is carefully added to urine in the usual wineglass test. Any case associated with an inflammatory process in the genito-urinary tract, as evidenced by history, physical examination, or examination of the urinary sediment, is, of course, not included in the figures or in the discussion. The examination of the sediment of the cases under discussion is negative for casts and cells in essentially 85 per cent. So-called cylindroids were frequently found. In the small proportion of cases in which casts were found the finding was inconstant, and these cases did not tend to be more persistent than those without casts.

As far as possible these cases of albuminuria have been followed up, and we have observations for varying lengths of time, some of which run over five years. As far as is known none of the cases of albuminuria, which did not present other evidence of nephritis, so that the diagnosis of nephritis could be made at the time of the examination, has subsequently developed nephritis. It may be perfectly possible that some of the cases of albuminuria are actual early cases of nephritis, but there is, as yet, no evidence of this in our series of cases.

It has been of interest to re-examine groups of these same young men, with the idea of verifying the previous observations. Re-examination of 100 unselected students showed that 5 per cent. of these 100 had albuminuria at the time of the examination. However, it was not the same 5 per cent. which had albuminuria at the first examination. Three of the men presented albuminuria on both occasions, and two who presented albuminuria on the first examination were replaced by two who represented albuminuria on the second examination. It seems evident, then,

that albuminuria tends to occur at any routine examination in a rather fixed proportion of unselected young men.

The next step obviously was to ascertain if the group of men presenting albuminuria had any common characteristics. It was found that albuminuria was relatively rare in the best athletes; for example, less than 1 per cent. of candidates for the varsity sports presented albuminuria. These candidates were men picked from a large group of men, and represented a special type of physical fitness. When the range of selection was made wider, as occurred in the case of candidates for the freshman teams, the percentage was somewhat higher, approximately 2 per cent., but it did not reach the general average of 5 per cent.

In one group of 662 young men blood-pressure readings were taken both standing and recumbent; 12.8 per cent. showed a systolic blood-pressure reading at one or both of these examinations over 140. These cases were subjected to further critical observation, with the conclusion that, except 1 case of nephritis, 1 case of obesity, and 2 cases of cardiac disease, the alteration of blood-pressure was inconstant and was to be associated with the nervous disturbance attendant on the examination, and these cases presumably represented types of labile blood-pressure. Nevertheless, although an abnormal systolic blood-pressure detected at a single examination seems to be of no significance, it was found that the incidence of albuminuria was twice as great in this group with labile blood-pressure as in the total group.

It is of considerable interest that there is also a variation in the frequency of albuminuria when judged from the point of view of bodily statics. If one classifies the posture of the students, as has been done by Dr. Lloyd T. Brown, one finds there is three times as great a percentage of albuminuria among the students who stand poorly as among the students who stand well. It should be added that 80 per cent. of the students were regarded as standing poorly, and 20 per cent. as standing well. These observations confirm the previous observation that those who are particularly physically fit, as the athletes, show less tendency to albuminuria than those who are not so completely physically equipped for athletics. It has been argued by some writers that

this particular form of albuminuria has some relation to the posture of the body, and our observations confirm this, but only to the extent that albuminuria is more frequent in those with poor posture than those with a good posture.

The individual cases of albuminuria have been studied with particular reference to the time of occurrence of the albuminuria. These cases divide themselves into three groups: Group 1 consists of those who show albuminuria at any and all examinations of the urine. Group 2 consists of those who show albumin during the daytime, much more marked after exercise, and not at all in the morning on getting up. Group 3 consists of those who may occasionally show albuminuria, although it has no demonstrable relation to amounts of exercise, etc. The second group is by far the largest group, and represents the usual type. The amount of albuminuria present seems to depend upon the amount of physical activity. The amount of albumin can be varied very easily by the quantity of exercise taken. After ordinary hard exercise it is not infrequent in this type of case to find an amount of albumin that is, at first sight, rather alarming. It may amount to  $\frac{1}{4}$  of 1 per cent. Certain of these individuals have been selected for careful intensive study. They have been sent to a hospital and the usual observations have been made on renal function by the phenolsulphonephthalein test, by the chemical study of the blood for blood nitrogen, blood urea, blood chlorids, and the  $\text{CO}_2$  combining power, etc. All these investigations were negative.

As the cases of albuminuria were observed, there was a marked tendency for the condition to disappear. Unfortunately, I have not the exact figures of the decrease of frequency of albuminuria. Among freshmen at Harvard University, with an average age of eighteen, the percentage of occurrence is 5. In another group of unselected upper classmen, with an average age of twenty, the percentage of occurrence was 3.5. It was impossible, however, to predict the outcome in any individual case. One particularly husky young man still has just as much albumin after exercise as he had five years ago, and he has been in perfect health during all that time. Cases have been followed who were encouraged to participate in formal athletics, as well as those

cases who did not participate in athletics. No difference could be seen in the condition. There were cases in which albumin persisted, as well as in which the albuminuria cleared up, whether they exercised violently or did not.

Nor was diet found to have any essential influence upon the condition. Some cases abstained very largely from meat, and it was not found that these cases showed any greater tendency to be free from their tendency to albuminuria than those cases who ate the usual diet. In all cases it has been customary to advise the avoidance of excessive ingestion of meat.

It was our experience usually that the general practitioners and also men skilled in internal medicine did not recognize this condition of temporary albuminuria of adolescence. This condition caused a great deal of alarm in many instances, and has been the reason why observation of the effect of certain drastic restrictions of diet and of exercise have been possible, because the family physicians of the young men have advised rigorous attention to diet or exercise.

Nevertheless, viewed from our considerable experience, this condition has not demonstrated itself to warrant any particular measures. It may not be, perhaps, a normal phenomenon of adolescence, because it does not occur in the boys who possess the best standards of physical health. It does occur so frequently in otherwise healthy boys of average physique that it should be discounted as an evidence of disease in the absence of other evidence of renal damage. Albuminuria should, of course, indicate a careful search for possible nephritis. But even persistent albuminuria is not incompatible with a clean bill of health, especially when albumin is absent after rest in bed and is present in varying amounts depending on the amount of physical exertion. Albuminuria in young men has been the cause of much needless alarm. It should be recognized as an abnormal finding, perhaps, but generally temporary, and not of a nature to warrant interference in any way with normal activity of these young men.



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MASSACHUSETTS GENERAL HOSPITAL

### ASTHMA, HAY-FEVER, AND ALLIED CONDITIONS

IT is very generally recognized that asthma, hay-fever, and several other diseases are due to a state of hypersusceptibility to protein, and that these various symptom-complexes are dependent upon the general condition of natural sensitization in man. This condition of natural sensitization includes a number of so-called diseases formerly regarded as clinical entities, but now thought of simply as various manifestations of one common underlying principle. When the manifestation is in the eyes and nose the hypersusceptibility is generally to one or another of the plant pollens, and the condition is called hay-fever. When the manifestation is in the lungs the hypersusceptibility may be to a variety of foreign proteins, or may be to some chronic bacterial infection, and the condition is called asthma (extrinsic and intrinsic respectively).<sup>1</sup> When the manifestation is in the skin the hypersusceptibility may be due to a wider range of substances, and the condition is called urticaria. Besides these three more or less typical examples, there are a few cases with symptoms of gastro-intestinal or subcutaneous origin, which should probably be included—cases of vomiting, diarrhea, and abdominal pain following the ingestion of certain foods, or cases of angioneurotic edema which often follow the ingestion of food.

The theories as to the causes and mechanism of these diseases, or rather of the fundamental hypersensitive state, are ill-defined and founded on relatively few facts, and it is, therefore, but natural that they should change.

However, it is necessary to understand these few facts in order to study and treat the condition properly.

<sup>1</sup> Rackemann, F. M.: A Clinical Study of 150 Cases of Bronchial Asthma, *Archives of Internal Medicine*, 1918, **xxii**, 517-552.

The facts which we have are these:

First: Certain cases of asthma, hay-fever, or urticaria, etc., have a very definite relation to some one or other definite protein substance, in that when the patients come in contact with this substance, either by direct contact or by inhalation or by ingestion, they wheeze, or sneeze, or itch, etc., and when not in contact with these substances they have none of these symptoms and are well. Second: When a minute quantity of this substance in soluble form is brought in contact with the skin or mucous membrane of the patient a violent local reaction takes place. Third: Repeated injections of a solution of this foreign protein substance will, in the majority of cases, bring about relief of the clinical condition; just as total avoidance of the substance will also give relief. From these three facts it is seen that there exists in the individual patient a marked hypersusceptibility to the foreign protein in question.

This hypersusceptibility is very comparable to the exquisite hypersusceptibility of the guinea-pig artificially sensitized to some foreign protein, as, for example, horse-serum. Not only are the symptoms presented by the patient in an attack and by the guinea-pig after the second dose of horse-serum very similar, but the quantity of the protein substance necessary to produce these symptoms is in each case minute and far below the amount necessary to produce any symptoms in normal individuals. On these accounts asthma, hay-fever, and urticaria have come to be considered as anaphylactic in nature.

Between anaphylaxis in animals and the condition of hypersusceptibility in man there are at least two differences. The first of these is the fact that guinea-pigs which recover from the shock following the second dose of horse-serum cannot be affected by a subsequent dose of horse-serum, provided this subsequent dose is given within a period of ten days. But during the treatment of asthma and hay-fever, cases are constantly seen which present marked local, and occasionally general, reactions to the particular protein to which they are sensitive, and with which they are being treated; and this in spite of the fact that they have already had just such a mild reaction within,

perhaps, a five-day period. In other words, the phenomenon of anti-anaphylaxis, well known in animals, is not seen in man. Second: Natural sensitization is usually multiple, whereas an animal sensitized artificially is specifically sensitized to that protein used for the sensitizing dose, and on reinjection will react to that protein and to no other. Furthermore, natural sensitization in man is, according to Cooke and Vander Veer,<sup>1</sup> encountered in about 10 per cent. of all individuals, while, as far as we know, it is never encountered in animals.

Between natural and acquired sensitization in man there are striking differences (Longcope).<sup>2</sup> Natural sensitization is usually multiple and is inherited, according to the Mendelian laws (Cooke and Vander Veer). Acquired sensitization is always single and specific. A more important difference on which there is lately being placed more and more emphasis is that in acquired sensitization in man, as characteristically shown in serum disease following the use of various antisera, there is a well-marked development of circulating antibodies (precipitins, anaphylactines, etc.), whereas in natural sensitization there is, in spite of numerous attempts to demonstrate them, no such development of these circulating antibodies.<sup>3</sup> Recent experiments in this clinic have shown that even after constitutional reactions incidental to the treatment of hay-fever and asthma no circulating antibodies are demonstrable in the blood.

From all this it seems reasonable that the underlying immune processes of hay-fever and asthma are probably not the same as those processes underlying both the ordinary anaphylaxis in the

<sup>1</sup> Cooke, R. A., and Vander Veer, A.: *Human Sensitization*, *Journal of Immunology*, 1916, 1, 201.

<sup>2</sup> Longcope, W. T.: *Susceptibility of Man to Foreign Proteins (Harvey Lectures)*, *Amer. Jour. Med. Sci.*, 1916, clii, 625.

<sup>3</sup> Cooke, R. A., Flood, E. P., Coca, A. F.: *Hay-fever. The Nature of the Process and of the Mechanism of the Alleviating Effect of Specific Treatment*, *Journal of Immunology*, 1917, ii, 217. Walker, J. C.: *Complement Fixation and Precipitin Reactions with the Serum of Bronchial Asthmatics who are Sensitive to the Proteins of Wheat, Horse Dandruff, Cat Hair, and Bacteria, Using these Proteins as Antigens and the Cutaneous Reaction as an Index of Sensitization, Study xii*, *Jour. Med. Research*, 1917, N. S., xxxi, 243-266.

animal and artificial, acquired sensitization in man. In a recent article Cooke<sup>1</sup> suggests that the condition of sensitization in man consists of an idiosyncrasy to various proteins: that these foreign proteins do not act as antigens, because they apparently produce no antibodies.

To date we know very little of the processes underlying the condition of natural sensitization in man, but the recent work outlined above would seem to indicate that the condition is less of a true anaphylactic nature than we have in the past five years been accustomed to think.

How do these theories and a knowledge of the underlying facts help us in diagnosing and treating cases belonging to this group, for example, cases of bronchial asthma? If we assume that some foreign protein substance (including bacterial proteins) is the basis of the condition, diagnosis consists in trying to identify this substance. Treatment will be planned and carried out in a much more intelligent way if the underlying principles are borne clearly in mind.

First, as to **diagnosis**. Each new case of suspected idiosyncrasy to foreign protein should have a very careful history. This history should include not only the character of the attacks themselves, but the periodicity and duration of these attacks, with especial reference to at least the following three points; (1) Season of the year, (2) change of residence or relation to locality, (3) relation to atmospheric conditions, including dampness, temperature, and wind direction.

The family history with regard to asthma, hay-fever, or food idiosyncrasy is very important, as it has been shown that the patients with idiosyncrasy to some foreign protein apparently inherit the tendency to this idiosyncrasy in at least 55 per cent. of the cases, whereas patients whose symptoms are probably due to bacteria inherit the tendency in only 10 per cent., so that a positive family history is a definite suggestion that a patient is susceptible to some foreign protein.

While of all tests and of all methods for studying these pa-

<sup>1</sup> Cooke, R. A.: Allergy in Drug Idiosyncrasy, *Jour. Amer. Med. Assoc.*, 1919, 73, 759.

tients the history is perhaps the most important and oftentimes is quite sufficient, yet we have another method of diagnosis. We know that patients who are susceptible to foods, animal dusts, and pollens will react positively when a solution of the protein is applied to a scratch on the arm. A skin test may be done in two ways, either by applying directly the purified protein to a drop of diluent on the arm and scratching lightly through it (cutaneous test), or a solution of the protein in high dilution and in definite quantity may be injected between the layers of the skin (intradermal test).

The results of the two tests are usually the same. The intradermal test is much more delicate. The cutaneous method, much easier technically, is often interpreted only with some difficulty. The chemistry of some proteins is such that they are not available in solutions which are entirely innocuous when injected into the normal skin, and hence the intradermal test has a limited application.

What proteins are used as a routine in the study of these cases? From what has gone before, it is obvious that we should be guided by the history in making intradermal tests. If pollens, food, or animal dusts are suggested, the skin tests of these substances should be done carefully and in greater assortment than the other proteins, but several proteins are so commonly causes of asthma that it is felt that their routine use is indicated in each case. The list of routine proteins should include:

- Ragweed.
- Horse hair.
- The split proteins of wheat.
- Egg-white.
- Goose feathers.
- One meat, as beef.
- One fish, as codfish.

In addition to this routine list other proteins can be added without limit. In this connection it should be borne in mind that none of these protein substances can be absolutely relied upon until such time as each particular protein preparation has given a definitely positive skin test in some patient whose experience

was entirely compatible with this skin test. Until such a positive skin test has been seen we cannot with certainty say that a negative test with that protein rules out a corresponding foreign substance (food, etc.) as an etiologic factor.

For the intradermal tests, our selection is limited to those proteins easily obtained in bland solutions. This group includes especially all the pollens, the white of egg, whole milk, the sera of animals. We have used meat broths from the kitchen in a numbers of cases, but have never seen a positive test. For these intradermal tests it is our practice to standardize the solutions according to their total nitrogen content. For the tests, solutions containing in 1 c.c. 0.02 mg. of nitrogen are used in each case.

In the study of each case another matter cannot be too strongly emphasized—the necessity of a careful and complete physical examination.

Further comment on these several points will be made in the discussion of cases which follows:

The first case is that of the man or woman of twenty-eight who has had hay-fever for sixteen years; whose father or mother has hay-fever or asthma or is poisoned by some food, as lobster or strawberries; whose hay-fever is limited in time from the day of onset in the middle of August to the first frost in late September (a period identical with the presence in the atmosphere of ragweed pollen) and who is entirely well at other times of the year.

The correct diagnosis in such a case can be made in five minutes, and the positive skin test to ragweed pollen extract is almost superfluous except that it proves the diagnosis and completes the picture.

Unfortunately, not all cases of asthma or urticaria are as easy of diagnosis, and the vast majority of patients in this clinic require extensive and careful study. We have been in the habit of testing them with numbers of food proteins in order to try to determine whether or not some food might be important in the etiology of the condition. These tests are often interesting and important. However, in a great many cases it is evident from the

history that diet has little or nothing to do with the case in question, as, for example, when a patient has been on a general diet for some time and has attacks of whatever nature at only very long intervals, which attacks are not preceded by the eating of any unusual food. Another case will give a history of having been on an exclusive milk or other very restricted diet for a number of weeks, during which time the symptoms remain unchanged. If, on the other hand, symptoms follow the ingestion of certain foods or come on a special day of the week or on holidays, and the patient gives corresponding and compatible skin tests, it is more than probable that special food is the cause of the attack.

In discussing the management of complicated asthma the history of a particular case is brought to mind. This man of forty-five had had asthma for ten years, during the last two of which it was practically steady throughout the year. A careful history of the early period of his asthma in comparison with the history during the preceding few years brought out the fact that he had suffered from hay-fever during August and September for twenty years, and that about ten years ago this hay-fever led to asthma in August and September, and about two years ago the asthma for the first time exceeded the bounds of the hay-fever season. This man presented on physical examination the characteristic appearance of emphysema. He raised considerable purulent sputum, but at the same time gave a definite skin test to ragweed extract. Largely on the basis of his history it was decided that the asthma was now (he was seen in December) largely of bacterial origin, but probably depended on an original background of hypersusceptibility to ragweed. Consequently, this year the man has been treated vigorously with ragweed pollen extract in July and August, with the result that his September asthma is very much improved, and the chance of overcoming the bacterial infection of his bronchial tree is thereby very much greater.

Sometimes in doing a number of skin tests as a routine one or more of these is positive. These findings are always striking and demand great care in their interpretation. It is felt that

unless careful investigation of history or daily experience can reveal some explanation, these positive tests should be regarded merely as isolated observations, the significance of which is at the moment unknown. For example, an Italian was found to give a typical skin test to oat protein. It developed that this Italian had never eaten oats, that nothing in his history suggested a food cause for his asthma, and that he hardly knew what oats or oatmeal were. It would have been ridiculous to advise this man to avoid oats and oatmeal, because as far as could be ascertained he never had eaten these foods. The significance of the test in this case was therefore unexplained.

Another practical point is the family history. Other things being equal, if the patient's father or mother or brothers or sisters have ever had hay-fever, asthma, or hives, there is that additional evidence that the cause of the patient's condition is of extrinsic rather than intrinsic origin.

A third point of practical importance is the necessity of examining these patients physically and very carefully. One case is recalled which, originally thought to have a food asthma, had been treated on this basis for several months. Avoidance of the particular food did not relieve the symptoms, but did help to produce a considerable loss of weight. When finally seen and studied the general condition was obviously poor, and somewhat late in the study a physical examination revealed evidences of pulmonary tuberculosis which were quite definite, and a few days later, following the administration of potassium iodid, tubercle bacilli were found in the sputum and the case was at once transferred to a sanatorium.

Another patient, a woman of fifty, was seen on the ward. She had had practically continuous asthma for the past fifteen years which had resisted all attempts at relief. It was brought out that her asthma was very much worse on exertion, and when she remained quiet or when during an attack she sat quite still in a chair the dyspnea improved markedly. In bed in the hospital ward she was more free from asthma than she had been for a long time. She came in with a blood-pressure of 220, and a pulse slightly irregular and of rather poor quality. The car-

diac area was increased. After a week of absolute rest the blood-pressure had dropped from over 200 to 125 and she was much improved. She was given small doses of digitalis because it was felt that a myocardial weakness was at least a very important factor in her asthma. On discharge she was advised to lead the life of a cardiac patient, and a letter received two weeks later reported her condition excellent so far as asthma was concerned.

Another striking example illustrating the importance of physical examination was a woman who had asthma and in whom an abdominal mass was easily palpable. There were no symptoms pertaining to this mass. It proved to be an ovarian cyst; was soon removed at operation, and she remained entirely free from her asthma for a number of months. The cure of her asthma was not complete, but the temporary improvement was great, and it was felt that the chances of her ultimate cure were thereby rendered greater and justified the operation. In this connection the importance of infected teeth and tonsils, the importance of treating constipation and other abnormal bodily functions should be emphasized.

The treatment of these cases is of greatest interest and importance. When once the cause of asthma or urticaria, etc., has been found, there are two courses open. Either the patient can avoid entirely the foreign protein in question or desensitization treatment with the foreign protein can be undertaken. The question of avoidance is important because, should the patient react to several foods, for example, several cereals, at the same time, which happens not infrequently, avoidance of all these substances is not only difficult to carry out, but will eventually undermine the patient's nutrition. And in these cases it is largely a question of study and trial with a view to identify and eliminate the one or two cereals most at fault.

Cases reacting to horse hair, who are much worse when the wind is in a certain direction and blows the horse emanations from the stable to the house, are often entirely relieved of asthma by moving to another house, perhaps not over half a mile distant.

The desensitization treatment is limited to those proteins which can be obtained in sterile bland solutions. Cereals, for example, are soluble only in relatively strong alkali and in alcohol. To inject a solution of them in any quantity would probably entail a disagreeable subcutaneous inflammation due to the diluent.

The desensitization treatment, therefore, finds its widest application in cases of hay-fever and in horse asthma, rarely in egg or milk asthma. The condition of hay-fever is an idiosyncrasy to ragweed pollen. No antibodies are produced in the disease; the treatment is quite different from any immunizing process, as, for example, vaccination against typhoid, and although we do not know the full details of what happens in the organism, we attempt to overcome the idiosyncrasy by the injection of gradually increasing doses of the protein. In this clinic in the treatment of hay-fever the first dose is arbitrarily set at a total quantity of ragweed extract containing 0.0001 mg. of nitrogen (the dilution is unimportant). Succeeding doses are given at five- to seven-day intervals, and are regulated according to the local reaction caused by the preceding dose. The treatment is begun about six weeks in advance of the hay-fever season; the object is to inject as large a quantity as possible of the extract into the patient, hoping to reach, at the usual time of onset of symptoms, a dose which contains 0.2 mg. of nitrogen, or, as expressed by many authors, a dose of 1 c.c. of the 1 : 100 solution. If the patient remains free of symptoms in spite of the fact that the time for his former hay-fever is overdue, further treatment is discontinued. The solutions usually are extracts of pure pollen in salt solution which contains N/200 NaOH together with 0.5 per cent. phenol.

The local **reactions** in the course of this treatment consist of a rather large, red, intensely itchy swelling at the site of the injection, which spreads sometimes 5 inches in all directions, and is raised perhaps  $\frac{1}{4}$  inch. Sometimes patients will have a general reaction. These general reactions are usually mild, consisting merely of a temporary increase of hay-fever, with a sensation of tightness in the chest and with a marked swelling in the arm.

At times, however, they are severe and alarming to both patient and physician. Like the mild reactions, they come on within ten minutes after the subcutaneous dose, and may progress to complete collapse, and the author has heard indirectly of one death. These severe symptoms are exactly comparable to the symptoms of anaphylactic shock in the guinea-pig with intense expiratory dyspnea, marked fall in blood-pressure and temperature, subcutaneous edema, and general prostration. The treatment for the reaction is always adrenalin (0.7 to 1 c.c. of a 1 : 1000 solution of adrenalin chlorid) which should be given subcutaneously.

Regarding the cause of the reactions we know little. They usually occur when, in the face of a well-marked reaction at the preceding treatment, there is a considerable increase in the dose; but, unfortunately, they also sometimes occur from a repetition of the smaller dose without apparent reason. In these latter cases they are rarely severe.

Although we know nothing of what effect these reactions may have on the body as a whole, we do know that serum disease (the reaction seven days after an injection of a foreign serum) is accompanied by a definite disturbance of the whole metabolism,<sup>1</sup> and attacks of urticaria<sup>2</sup> in hypersensitive individuals have been found to be associated with severe renal insufficiency, so that pollen and other protein reactions should be distinctly avoided if possible.

Treatment in hay-fever if carried out correctly yields fair results; the first year about 75 per cent. of the cases show great improvement and 10 to 15 per cent. are entirely relieved of all symptoms. In the second and third year of treatment the results are slightly greater.

The desensitization treatment of asthma is carried out along the same lines as that of hay-fever, has the same pitfalls and

<sup>1</sup> Rackemann, F. M., Longcope, W. T., and Peters, J. P.: The Excretion of Chlorids and Water and the Renal Function in Serum Disease, *Archives of Internal Medicine*, 1916, xviii, 496-504.

<sup>2</sup> Longcope, W. T., and Rackemann, F. M.: Severe Renal Insufficiency Associated with Attacks of Urticaria in Hypersensitive Individuals, *The Journal of Urology*, 1917, i, 351.

dangers, but, on the other hand, yields results which are, on the whole, much more satisfactory.

So far little has been said as to the treatment of asthma when this is probably due to bacteria. There are two methods of treating a case when bacteria are considered to be the cause of the disease. The first consists in removing the focus of infection either by operation or by means of general hygienic measures, change of climate, etc., to clear up the infection by "medical means." The second method concerns the use of vaccines. These may be stock vaccines or autogenous vaccines, and to date we have no very accurate criteria as to which to use or how to use them. Walker<sup>1</sup> employs usually, for making vaccines, the predominant organism in the patient's sputum and claims fair results. No other extensive work has been reported on this subject and our present methods are, therefore, rather empirical. In 2 of our cases vaccines made by washing off the entire growth from a dextrose-agar slant planted directly with the patient's sputum have yielded fair results. It is hoped later to use sputum vaccines in a much more accurate way and in a pure state.

To sum up: The condition of hypersusceptibility in man is probably a disease entity which includes a great variety of clinical conditions varying from hay-fever to asthma.

Second: The diagnosis of this condition as a whole is easy, but the diagnosis of the protein causing the individual symptom-complex is difficult. A careful history should be the foundation of the study. Skin tests should amplify and confirm this and indicate proper treatment. Physical examination will often reveal striking points.

Treatment consists of avoiding the protein in question or of desensitizing the patient to the protein. The results are usually satisfactory, but are attended with the danger of protein reactions unless carefully carried out.

<sup>1</sup> Walker, I. C.: The Treatment of Bronchial Asthma with Vaccines, Archives of Internal Medicine, 1919, xxiii, 220-234.

## CLINIC OF DR. JAMES H. MEANS

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### HYPERTHYROIDISM—TOXIC GOITER

It is my purpose to present a series of cases in which observations of the basal metabolism have been helpful either in diagnosis or in the determination of proper treatment. A word as to what is meant by basal metabolism is in order, but before we come to that let me make a few introductory remarks.

It has long been recognized in medicine that a patient's heat regulation is of vital clinical importance. The temperature curve is assiduously followed with all patients with acute infections. The disturbance in heat regulation resulting in fever is regarded as the sign par excellence of the severity of the febrile patient's disease. But is not heat production quite as fundamentally interesting as heat regulation? The body temperature tells us whether or not the relation of heat production and heat loss is normal. A patient with fever may or may not have an increase in heat production, but he does in any event have either a relative or absolute diminution in heat loss. Otherwise his temperature would not rise. But in certain afebrile diseases, on the other hand, one finds a great increase in heat production, with no increase in body temperature, this being due to the fact that although the heat production is increased, so also is heat elimination; and thus, in spite of the rise in heat production, body temperature remains normal because the extra heat is eliminated.

This matter of heat production then has a definite clinical bearing quite as much as does body temperature; but while temperature can be determined in a moment with the clinical thermometer, heat production can only be measured with

rather complicated apparatus. One way to measure it is to use the so-called calorimeter, an instrument consisting of a chamber in which the patient is placed and in which the heat he gives off is actually measured through the rise in temperature imparted to a known volume of water flowing through a radiator within the chamber. This method is quite beyond the possibilities of an ordinary clinic. A second method is the measurement of the patient's gas exchange. When food substances undergo combustion within the body they yield the same amount of heat as when burned in a flame. From the ratio of oxygen absorption to carbon dioxid elimination can be learned the kind of food being burned, and by use of the calorimetric bomb has been learned the calorific value of oxygen when various food substances are oxidized. Therefore, if we know a patient's gas exchange, we can calculate his heat production. This procedure is called indirect calorimetry, as opposed to direct calorimetry when the large calorimeter is used.

The gas exchange can be measured by a variety of apparatus, some of which are well adapted to clinical use. The one recently devised by Benedict is probably as good as any. Into this apparatus, which is a closed system of tubes, the patient breathes, and the  $\text{CO}_2$  he gives off is collected in soda lime bottles, while the oxygen he uses is measured from the shrinkage in total volume.

Having determined the patient's heat production, how are we to judge of its normality? It is well known that various factors, such as rest, bodily exercise, etc., increase heat production. However, it is also known that if we take persons at complete rest and in the postabsorptive condition, that is, ten or more hours after the taking of food, their metabolism will be remarkably constant. It is the heat production under such circumstances that we term "basal metabolism."

In individuals of different sizes the heat production will vary, but nevertheless we can still decide whether in any given subject the metabolism level is normal, for, as was discovered by Rubner, the heat production is proportional to the surface area of the body. In terms of their surface area a mouse and an

elephant have essentially the same basal metabolism. The area of the human subject, thanks to DuBois, can be readily determined from the height and the body weight.

Let us now consider the bearing of all this to clinical medicine. I have said that just as certain diseases, namely, infections, are manifested chiefly by a rise in body temperature, so too are certain other diseases characterized by an increase in heat production without rise in body temperature, by a rise, in other words, of basal metabolism.

What are these diseases where heat production is increased? By far the greatest increase is found in Graves' disease. Here we sometimes find the basal metabolism as much as double the normal, and that with no increase in body temperature. In leukemia also we find a marked rise, and in pernicious anemia a somewhat less striking one. In a variety of other conditions, such as acidosis, polycythemia, and hyperpituitarism, there may be some slight increase in heat production.

We also in certain other diseases find a decrease in the metabolism. Just as the most striking rise was in Graves' disease, so the most striking fall is in myxedema, while a less marked fall may be found in hypopituitarism.

So characteristic of thyroid disease are changes in the basal metabolism that personally I believe that in the metabolism level we have a functional test of that gland, increase of metabolism meaning hyperthyroidism, and decrease hypothyroidism, provided, of course, that other diseases that alter basal metabolism are excluded.

In following the course of Graves' disease I believe that the basal metabolism furnishes the best index of the intensity of the intoxication that we have, and that it is a factor we always must have if we wish to treat this disease properly. Just as in following a case of pneumonia we study the temperature, pulse, and respiration curves, or in nephritis, the blood-pressure, water, salt, and nitrogen balance, so in thyroid diseases our chart should consist of metabolism curve, pulse curve, and weight curve, these being, without question, the three most important factors.

In the present clinic the cases I have to show are those of

patients either with suspected or proved thyrotoxicosis. In borderline cases a metabolism determination serves well as a method of differential diagnosis between a simple neurosis, let us say, and a case of mild hyperthyroidism, the former having a normal metabolism, the latter an elevated one.

I will show a few of these borderline cases first. The basal metabolism level, let me say, is always expressed as a percentile increase above the normal. A normal man of twenty-five produces 39.5 calories per square meter per hour. A man of the same age having a metabolism of 79 calories per square meter per hour we should say had a metabolism of plus 100 per cent., one with 19.75, minus 50 per cent., etc.

Of the borderline group I will first show the case of Mr. P. R. N. (Laboratory No. 1, Hospital No. 195,258, W. S., E. M.). This patient has had quite a distinguished career from a metabolism point of view. He first entered the Massachusetts General Hospital on May 1, 1914. He was a tall, thin, stoop-shouldered individual with definite visceroptosis. His chief complaint was loss of appetite and general weakness. He also had some indigestion and a certain amount of nervousness and palpitation of the heart. His thyroid gland was very slightly enlarged, but he had no eye signs or tremor.

On June 10, 1914 I determined his basal metabolism and found it to be but 4 per cent. above the normal, and on the day following it showed no variation from the normal. I thereupon expressed the opinion that he was not suffering from hyperthyroidism and that treatment should be directed toward the correction of his ptosis rather than toward his thyroid gland.

Our clinicians, however, at that time did not regard the basal metabolism determination as a functional test of the thyroid very seriously, and they still felt that the man had a toxic goiter. Accordingly, on June 18, 1914, the superior thyroid arteries were ligated under novocain. The patient made an uneventful convalescence and left the hospital.

He was not heard from again until the latter part of 1915, when DuBois informed me that he had turned up at the Russell

Sage Institute, and that they had made some studies of the metabolism there. An account of their studies appears in DuBois' paper on The Metabolism in Exophthalmic Goiter, where he is designated Case 5, "Peter N." He gave them a history that since his discharge from the Massachusetts General Hospital a year before he had not been any better. On April 14, 1915, DuBois determined his basal metabolism in the large calorimeter and found it to be minus 2 per cent. At that time they found that he still had a slight soft enlargement of the thyroid and some tremor of the fingers. Otherwise he presented essentially the same picture as when seen by us.

In the spring of 1916 he again turned up at the Massachusetts General Hospital in our dispensary. He had exactly the same symptoms as when seen two years before, very stoop shouldered, thin, with marked visceroptosis. I felt then as I felt before, that he was not suffering from hyperthyroidism and that his whole condition was due to his faulty posture and ptosis. He was referred to the orthopedic department for treatment.

This case is particularly interesting in showing that the basal metabolism determination does have a very definite rôle in the differential diagnosis of borderline thyroid cases. If attention had been paid to the original metabolism determination in this case, he would have been saved a surgical operation, and in all probability would have been started on the right type of treatment two years earlier than he actually was.

I will now show another case where the metabolism determination has been useful in judging whether any thyrotoxicosis was present. Miss M. A. W. (Laboratory No. 18, Hospital No. 201,409, E. M.), a graduate nurse thirty-one years of age, who had had an enlarged thyroid for sixteen years, and who, five years before I saw her, while overworking in the training-school, developed some slight signs and symptoms of hyperthyroidism. In spite of these she finished her training course, and then for about a year was under treatment for hyperthyroidism, during which time she took considerable rest and was also given quinin hydrobromid. I saw her first on April 22,

1915, and made a determination of the basal metabolism and found it to be plus 9 per cent. She was then working as a graduate nurse and was feeling entirely well and had no signs or symptoms of thyrotoxicosis.

In October, 1916, I saw her again. In the interim she had developed some slight nervousness and a little palpitation. During the preceding summer she had rested considerably and had again taken quinin hydrobromid. She had decided that she was then well enough to go back to nursing. At that time she had a slight soft enlargement of the thyroid gland, no eye signs, and no tremor. I found the metabolism on October 23, 1916 to be plus 14 per cent. She was then under the care of a private physician in Boston, a man of high standing in internal medicine and one who had had a particularly wide experience in the subject of Graves' disease. I wrote to him and told him of my metabolism findings and expressed the opinion that Miss M. A. W., if thyrotoxic at all, was only very slightly so, that the prognosis was very good, and that if she avoided overworking she would probably require no other treatment. His reply to this is distinctly illuminating. He wrote me as follows: "I am most certainly interested in your experiments and have tried to follow them as well as I could outside the hospital, so that I should be most interested to read your pamphlets on the subject. Miss W. is, of course, a marked Graves' and it is a question whether she will be able to pull along without operation. She is much averse to having anything done, but I am afraid it will have to come in time." This opinion, bear in mind, was that of a man particularly skilled in the field of Graves' disease, and yet subsequent events have proved that the inference drawn from the metabolism determination was the correct one and that his clinical impression was entirely wrong.

I have seen Miss M. A. W. several times this spring (1919). She is perfectly well, has been nursing most of the time, and has nothing about her now to suggest hyperthyroidism. The value, therefore, of a basal metabolism determination for the differential diagnosis of hyperthyroidism is quite clearly illustrated by her case.

The next patient that I shall show illustrates a somewhat different point. Mrs. F. A. (Laboratory No. 26, Hospital No. 202,488, E. M.), a housewife of thirty-three, with negative past and family history, for some six months had had slight edema of her ankles and some dyspnea on exertion. On physical examination she showed a slight enlargement of the heart with a systolic murmur at the apex and tachycardia. She had no eye signs and her thyroid was not enlarged. Nevertheless, Dr. Paul D. White, who saw her and who felt that there was definitely organic heart disease, thought that possibly there was likewise an element of hyperthyroidism, and consequently a determination of the basal metabolism was made. On June 22, 1915 it was found to be plus 23 per cent.

In the spring of 1919 she came to the hospital again in response to a letter from me and gave the most interesting story that following her discharge in 1915 she had gradually developed rather slight but nevertheless typical symptoms of thyrotoxicosis, nervousness, tremor, increased sweating, etc. On April 9, 1919 I again determined her basal metabolism and found it to be plus 52 per cent.

This case is interesting because the metabolism observation of June, 1915 showed that she definitely was somewhat thyrotoxic at that time, and the subsequent history shows that she later developed the clinical picture of mild hyperthyroidism, and that when seen four years later she was more toxic than she had been before. She had had no treatment directed toward her thyroid in the interim. If due regard had been paid to the significance of the first metabolism determination, this patient might have been saved her subsequent increase in thyrotoxicosis.

Let us next consider briefly a case in which the diagnosis lay between a simple cardiac neurosis and a mild hyperthyroidism. Miss R. M. P. (Laboratory No. 158, Hospital No. 213,759, E. M.), a woman of twenty, with negative past and family history, who for five years for no known cause had had palpitation and dyspnea on excitement or exertion. She had also had attacks of precordial pain. Physical examination and all

laboratory tests were essentially negative. Dr. Paul D. White saw her and felt that her case was a reasonably typical one of irritable heart, but that he would prefer that hyperthyroidism be excluded. Accordingly, on March 14, 1917 a metabolism determination was made and showed a result of plus 5 per cent. On this basis hyperthyroidism we felt was properly excluded, and the patient was treated for her cardiac condition.

Another patient whose case is perhaps worth mentioning for a moment is that of Mr. A. C. (Laboratory No. 155, O. P. D. No. 219,070). He was a man of forty-nine, with marked exophthalmos, but with no thyroid enlargement, and with absolutely none of the usual signs or symptoms of thyrotoxicosis. His basal metabolism was determined on March 10, 1917, and was found to be plus 9 per cent. On the strength of this it was decided that whatever was the cause of his exophthalmos, he was not suffering from increased thyroid activity at that time. His condition in the spring of 1919 has been learned, and it has been found that his exophthalmos has remained exactly the same and that he has developed no signs whatever of Graves' disease. The conclusion as to the correct diagnosis, then, drawn from the observation of March, 1917 has been borne out by subsequent developments.

I will now take up just one more of the borderline cases or, I might better say, cases where metabolism determinations were made for purposes of differential diagnosis. Let me present the case of Miss M. G. C. (Laboratory No. 85, Hospital No. 210,992, E. M.). This lady was a librarian of thirty-five, with negative family and past history. She had had a swelling in the neck for ten years which had been getting bigger during the last year. She had had some palpitation and some slight dyspnea on exertion for a few months only. Physical examination showed no eye signs, no tremor, but did show the thyroid gland moderately enlarged, the right lobe being larger than the left, the whole being soft and presenting an irregular surface to palpation. No bruit could be heard.

The point in differential diagnosis here was: Was this a toxic or a non-toxic goiter? A metabolism observation was made on October 12, 1916, and the result was found to be plus 3 per cent. It was therefore decided that the goiter was a non-toxic one. This case illustrates, therefore, that in the presence of thyroid enlargement, when there is doubt as to whether thyrotoxicosis is likewise present, a metabolism determination forms an excellent means of differential diagnosis.

I will now pass to my second group of cases—those of true toxic goiter. In such the diagnosis, of course, is quite obvious without a determination of the basal metabolism; but what I want to bring out in this clinic is that to intelligently follow the progress of a patient with thyrotoxicosis it is necessary to follow the curve of the metabolism level. Impressions drawn from clinical signs, of the severity of intoxication, may be quite misleading, and especially misleading may be the clinical impression of the patient's progress. As I have said before, to my mind the clinical chart of the thyroid patient should consist of metabolism curve, pulse curve, and body weight curve. I shall show you today such charts in 8 cases and try to point out to you what an accurate way of following their progress metabolism determinations furnish. My remarks as to the effects of treatment will center chiefly about surgery and about *x*-ray treatment, these being the two forms of treatment that have been studied most carefully in our clinic.

First, let us consider a few patients who were treated solely by the *x*-ray, and of these we will first take up the case of Mrs. E. N. (Laboratory No. 48, Hospital No. 205,776, E. M.). This patient was first seen in January, 1916. She had apparently had severe Graves' disease for at least four and a half years. Several years before she had improved for a time on rest and quinin hydrobromid, but for the last eighteen months she had been getting steadily worse. She was exceedingly nervous and had considerable dyspnea and palpitation on excitement or exertion, and marked increase in sweating and a pathologically large appetite. Physical examination showed extreme exoph-

thalmos, marked tremor, and a moderate soft enlargement of the thyroid gland with a loud systolic bruit.

Her chart tells her story. On January 1, 1916 you will note that her basal metabolism was plus 82 per cent. She was kept in bed in the ward until into February, 1916, and x-ray treatment was given. This combined rest and x-ray treatment brought her metabolism and pulse down 20 or more points.



Fig. 210.—Mrs. E. N., photo taken June 9, 1916, at which time she had had two x-ray treatments.

Fig. 211.—Mrs. E. N., photo taken July 16, 1918, when she had had a total of eleven x-ray treatments.

It then remained essentially level up through January, 1917, at which time she had had six x-ray treatments. From that point on, however, we begin to see marked improvement. In May of 1919 she was still undoubtedly toxic; nevertheless a great deal less so than three years before. She was leading her usual mode of life and subjectively was quite comfortable. She had gained enormously in weight in spite of the fact that her metabolism was still 25 per cent. above normal, and actually presented a

definite picture of obesity. I should like to lay stress on this point because had I not known from her metabolism observation that she still was somewhat thyrotoxic, because of her obesity I should have been led to believe that she might be actually suffering from hypothyroidism and might even have given her thyroid gland therapeutically, which, of course, would have been exactly the wrong thing to do.

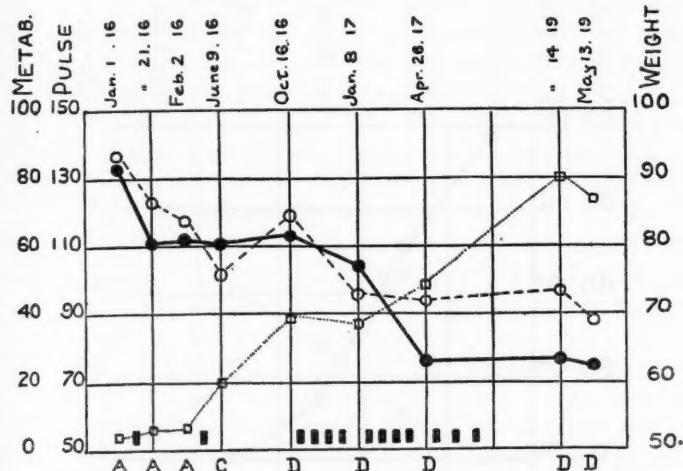


Fig. 212.—Mrs. E. N. In this and in succeeding figures basal metabolism is shown as a percentile increase above normal by a solid black line and dots; pulse, by an interrupted line and circles; weight in kilograms, by a dotted line and squares, and x-ray treatments, by black rectangles. *A* denotes that the patient was getting complete rest in bed at time the observation was made; *C*, partial rest, and *D*, that she was leading her usual life. This same notation will be used in succeeding figures.

Her chart as a whole is interesting, in that the pulse curve and metabolism curve throughout are essentially parallel, while the weight curve is essentially the reciprocal of these two curves. This is what one would expect; as the toxicity decreases, the weight should increase; but, as I can show in some of the charts that we have yet to look at, this is not invariably true. The parallelism of pulse curve and metabolism curve is very con-

stant, but the reciprocal relationship of weight to these two curves is not necessarily constant.

In regard to pulse curve and metabolism curve there is one more point which I should like to call attention to, and that is the fact that as we study these charts we will find that there are two definite types: one type in which the pulse curve runs very definitely above that of the metabolism, 10 or more points, and

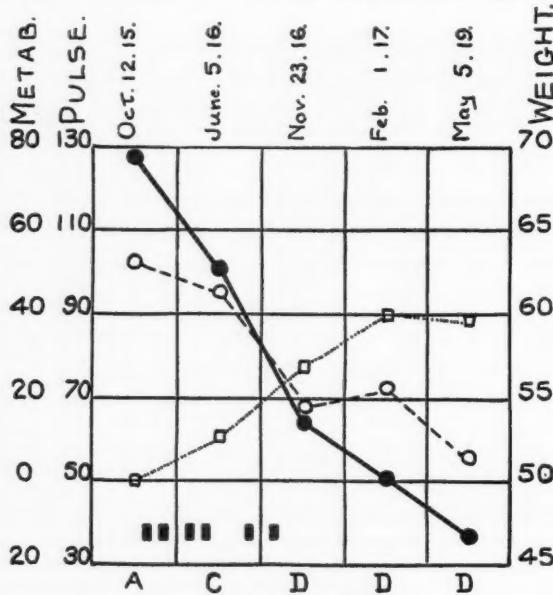


Fig. 213.—Mr. B. S.

a second type where the pulse curve either coincides with the metabolism curve or runs below it. This patient belongs essentially, at least during the first part of her career, to the latter type. A little later I will take up the significance of these two types in regard to treatment and prognosis.

I will next show the case of Mr. B. S. (Laboratory No. 33, Hospital No. 204,683, E. M.), a Hebrew patient twenty-four years of age, a barber by trade. He came to the hospital in

October, 1915, and presented the typical picture of Graves' disease—a moderate soft symmetric enlargement of the thyroid gland with a moderate bruit, definite exophthalmos, and marked tremor. These symptoms he had had for two years and they had gradually been getting worse. When I saw him first he had been obliged to give up his occupation because he could not hold a razor steadily enough to shave a man without cutting him. His metabolism on October 12, 1915 was 78 per cent. above the normal. He was started immediately on *x*-ray treatments, and, as his chart beautifully illustrates, showed a steady improvement, fall in metabolism level and pulse-rate, and a steady gain in weight. When seen this spring (1919) his metabolism was normal and he presented no signs whatever of thyrotoxicosis. He said that he felt perfectly well and that he had been working steadily for over two years.

This case illustrates, as well as any we have, a very toxic type of Graves' disease, with steady improvement and ultimately complete recovery following essentially no therapy whatever beyond six *x*-ray treatments.

I should add at this point, both in regard to this patient and the preceding one and also to subsequent ones, that have had *x*-ray treatments, that the method was to expose both thyroid and thymus glands to about two-thirds the erythema dose. The treatments were given usually from three to four weeks apart and were all given by or under the direction of Dr. George W. Holmes, the Roentgenologist of the Massachusetts General Hospital.

I will show another patient who also has received essentially no treatment but *x*-ray. Mrs. V. M. D. (Laboratory No. 135, Hospital No. 212,958, W. M.), a woman of thirty-nine years, with an unimportant past history, who for one year had had symptoms of mild thyrotoxicosis—slight nervousness and some dyspnea and palpitation on exertion. She showed very marked exophthalmos, slight tremor and a slight soft symmetric enlargement of her thyroid, with a faint bruit. On January 28, 1917 her basal metabolism was found to be plus 39 per cent.

The only previous treatment she had had was that for six months she had been taking quinin hydrobromid and for eleven days previous to this observation she had been in bed in the hospital ward. She was kept in bed for about three weeks, having had, as the chart shows, a fall in metabolism and a slight gain in weight. At home she grew somewhat worse and her metabolism rose to plus 47 per cent. on March 9, 1917, and so she was started on x-ray treatment. After seven treatments, on January 30, 1918, she had made a very marked improvement. She

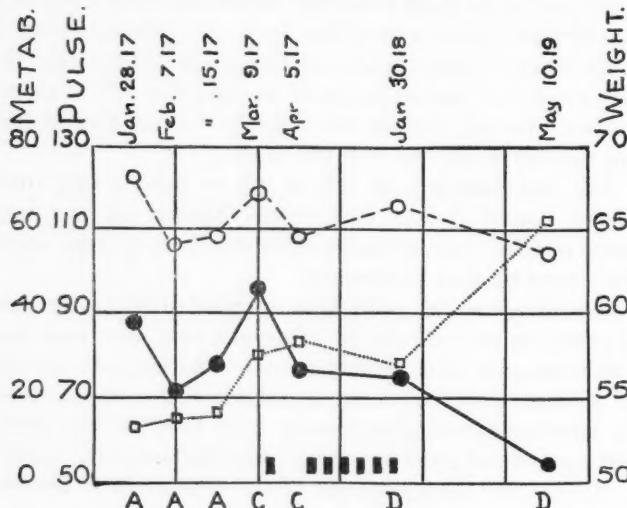


Fig. 214.—Mrs. V. M. D.

was doing light housekeeping and said that she felt well. Her metabolism, however, was still 25 per cent. above normal and she had quite a rapid pulse.

I again saw her on May 10, 1919, and she said that she felt very well indeed, and, furthermore, she no longer appeared thyrotoxic. She had had a healthy child since the observation of 1918, and was now caring for her family and nursing her baby. Her metabolism was plus 4 per cent., which is quite within normal limits, and she had shown a marked gain in weight.

This case, like the preceding one, appears to be a cure accomplished entirely by means of the *x*-ray. It is worth calling attention to the relation of pulse curve to metabolism curve in this case. In the two preceding cases the pulse curve has been more or less coincident with the metabolism curve; in the case of Mrs. V. M. D., however, it will be noted that the pulse nearly always runs some 25 points above that of the metabolism. My own feeling is that in this relationship between pulse and metabolism we have an indication which may throw some light on the rôle that the thymus gland is playing in any given case. It has been fairly well shown that practically all cases of Graves' disease have persistent thymi and that the thymus gland plays an important part in the causation of Graves' disease. Eppinger has claimed that there are certain cases, which he calls the vagotonic type, in which the thymus plays a more important part than it does in certain others, which he calls sympatheticotonic, the latter type having among other things a more pronounced tachycardia than the former. I do not care to enter into the controversy as to whether two such types actually exist, but I might say that from a careful study of such data as I have been able to collect there seem to be two reasonably distinct types, one in which there is an extreme elevation in pulse and a moderate elevation in metabolism, and the other in which there is an extreme elevation in metabolism and a moderate elevation in pulse. The charts which I am showing are all plotted according to a fixed scale as regards pulse and metabolism. The base line always represents normal metabolism and a pulse-rate of 50 and the top line a metabolism of 100 per cent. above normal and pulse-rate of 150. In the discussion that follows merely for the sake of convenience I am going to refer to the type where the pulse runs 10 or more points above the metabolism curve as belonging to the sympatheticotonic variety, and to those in which the pulse runs coincident with or below the metabolism curve as the vagotonic variety. Those like Mr. B. S. or Mrs. E. N. would be classed in the vagotonic group; while Mrs. V. M. D., on the other hand, who has a tachycardia out of all proportion to her metabolism elevation, would be classed in the

sympatheticotonic variety. My experience has been that the prognosis in the type with greater elevation in pulse than in metabolism is better than it is in the type with high metabolism and moderate pulse elevation. In the first of these types it seems to matter very little, in regard to end-result, whether medical or surgical measures are employed; in the second type, however, that with high metabolism and moderate pulse elevation, recovery may take place with *x*-ray alone, as did Mr. B. S., but, as in some of the cases I shall show later, operation may be necessary. The important point that I wish to make is that in the latter type the risk of operation seems to be greater, but also there is some evidence to show that this risk may be reduced by exposing the thymus gland to the *x*-ray before surgery is undertaken.

I will now show a case, that of Mrs. A. B. (Laboratory No. 93, Hospital No. 212,531, W. M., W. S.), who is also to be regarded as of the sympatheticotonic type. A glance at her chart will show that her pulse curve, though always strictly parallel with that of the metabolism, is always 40 or more points above it. She has, in other words, a moderate rise in metabolism, but an extreme rise in pulse-rate. I first saw her on October 27, 1916. Her history was that of typical Graves' disease of a very acute type. Two months before she had been perfectly well; then she developed slight nervousness, and on physical examination showed slight soft symmetric enlargement of the thyroid with moderate bruit. Her metabolism was plus 40 per cent. It was felt at that time that she was a rather mild case who would probably do well on *x*-ray treatment, but after four treatments there had been essentially no drop in the metabolism, though there had been a slight gain in weight and a slight fall in pulse. It was therefore decided to resort to surgery, and on February 14, 1917 a lobectomy was done by Dr. Charles A. Porter under gas and oxygen. The right lobe and isthmus and about a quarter of the left lobe of the thyroid was removed. Pathologic examination of the removed tissue showed hyperplasia of the follicles with frequent infolding of the epithelium

and also numerous bands of fibrous tissue with some areas of lymphoid cell infiltration. The anatomic diagnosis was struma parenchymatosus.

The patient made a good operative recovery, and on February 24, 1917 her metabolism was back within normal limits and her pulse had fallen some 20 points. From this time on

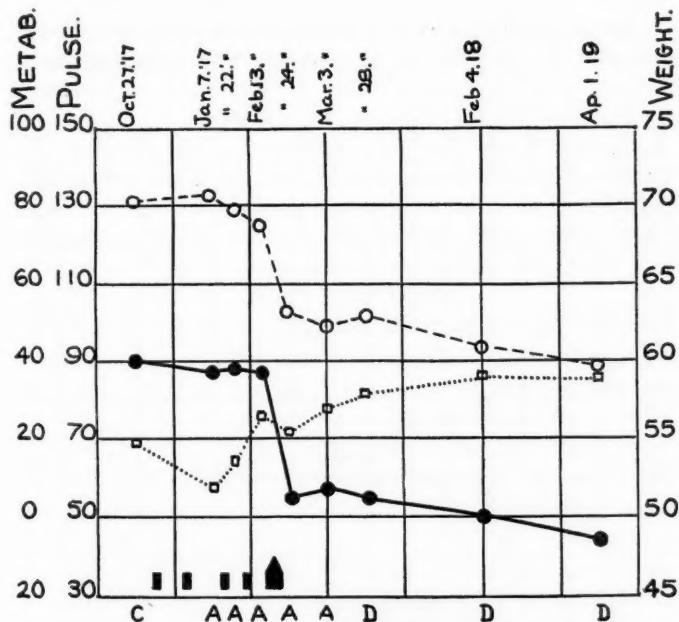


Fig. 215.—Mrs. A. B. In this and in succeeding figures a black triangle on a black square denotes a partial thyroidectomy.

she made a steady improvement, and when seen on April 1, 1919 she had been perfectly well for two years. She was doing her own housework for a family of 4 and showed none of the signs or symptoms of thyrotoxicosis. Her metabolism was minus 8 per cent. and she had gained considerably in weight.

I do not believe that in this case  $\alpha$ -ray treatment was given a fair trial; I think that very likely if it had been continued longer

that we should have gotten the same end-result. Nevertheless, it is only fair to the surgeon to say that operation accomplished perhaps a more rapid cure than would have been secured by medical measures. Belonging as she does to the sympatheticotonic type, she was a good operative risk and had an uneventful convalescence.

Let us pass to the case of Mrs. H. R. (Laboratory No. 71, Hospital No. 210,587, E. M. and W. S.). This patient, a

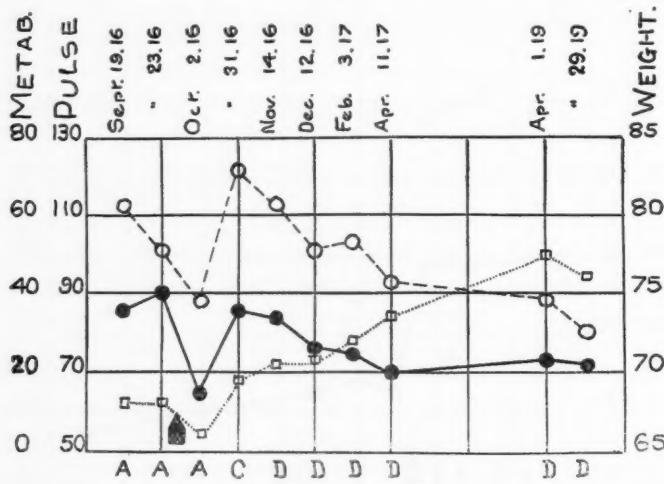


Fig. 216.—Mrs. H. R.

woman of thirty-seven years, had had the signs and symptoms of Graves' disease for some eighteen months. Her eyes were slightly prominent and she had slight tremor of the fingers. The thyroid showed a moderate soft symmetric enlargement. A glance at her chart will show that she too is to be regarded as of the sympatheticotonic type because her pulse curve runs anywhere from 15 to 20 points above that of her metabolism. Before coming under my observation she had received eight x-ray treatments, with apparently no very definite improve-

ment; therefore it was decided that surgery had better be resorted to, and after metabolism determinations on September 19 and 23, 1916, a lobectomy was done on September 25th by Dr. Charles A. Porter, under novocain. The right lobe was removed. The pathologic examination of the removed tissue showed essentially the same thing as that of Mrs. A. B., namely, hyperplasia of the follicles with some increase of the surrounding stroma and occasionally focal areas of lymphoid cells, and the same anatomic diagnosis of struma parenchymatosa was made. She stood the operation well, and on the second day of October, 1916 showed a metabolism of only plus 15 per cent. Later, however, after going home, she apparently had an increase in thyrotoxicosis and her metabolism returned almost to the level where it had been before operation. This, I might say, is quite a common occurrence. In many cases one finds a very striking drop immediately after operation, but, just as with this case, a recrudescence in the second to third month.

Without any further treatment this patient made a gradual improvement, and when seen this year (1919) she said that she had been following her usual occupation of housekeeping and that she felt very much better. She could not be called entirely recovered, however, for her metabolism was still some 22 per cent. above normal. Nevertheless, she had shown a marked gain in weight and a fall in pulse-rate and is undoubtedly a great deal better.

The next surgical case is that of Miss M. D. (Laboratory No. 125, Hospital No. 212,305, E. M., W. S.). She was a woman of twenty-seven years whom I first saw in December, 1916. She had had symptoms of Graves' disease for a year and a half—extreme nervousness, pathologically large appetite, marked sweating, loss of 30 pounds within a year, and considerable dyspnea on exertion. She had slight exophthalmos, a very well-marked tremor of the fingers, hot moist hands, and a moderate hard symmetric enlargement of the thyroid over which was heard a loud bruit. The right superior thyroid artery had been tied in May, 1916 at St. Luke's Hospital, New Bed-

ford, after which for a short time she had felt better. On entering the Massachusetts General Hospital she was put to bed and, as a glance at her chart will show, had a very marked progressive fall in both metabolism and pulse-rate. The chart will further show that her pulse curve always runs close to the metabolism curve and that she is therefore to be regarded as the vagotonic

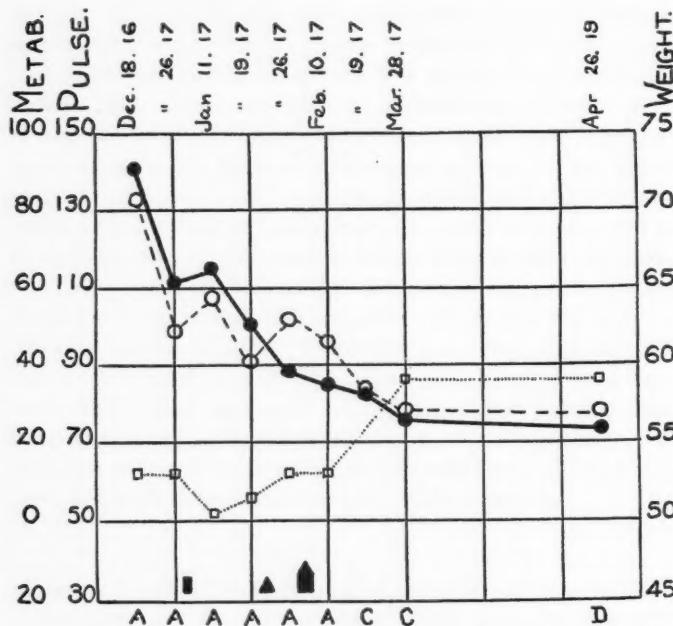


Fig. 217.—Miss M. D. The black triangle denotes a ligation of superior vessels. As before noted, the black triangle on the black square denotes a partial thyroidectomy.

type. She received one  $\alpha$ -ray treatment between the third and fourth metabolism observations, but it was then decided that it would be best to operate. On January 19, 1917 the left superior thyroid artery was tied under novocain by Dr. Charles A. Porter. She stood this well and showed a further drop of metabolism after it; so on January 30th Dr. Porter operated again,

and under novocain removed the entire right lobe and isthmus. The removed tissue showed follicular hyperplasia, many follicles of the fetal type, solid columns of cells with no lumen. There were also numerous papillary infoldings of the epithelium and wide bands of fibrous stroma, and throughout the whole gland a diffuse infiltration with lymphoid cells which sometimes formed actual lymph-follicles. The anatomic diagnosis was struma parenchymatosa. This patient continued to improve after her two operations, but I have the feeling from an extensive study of metabolism data that the *x*-ray treatment she had had before was definitely contributory to the success of the operation. She is definitely, I believe, of the type with marked thymus involvement, and I believe had she been operated upon outright without previous *x*-ray treatment that she would have been a not particularly good risk. Cases just like hers, where the metabolism has been high, out of proportion to the pulse, have frequently done badly when operated upon, and oftentimes died deaths resembling those seen in *status lymphaticus*.

Following operation this patient had no further treatment, and when seen on April 26, 1919 she said that she felt well and that she had been working as a domestic for two years. There was no clinical evidence of thyrotoxicosis, but her metabolism was still 23 per cent. above normal. She had gained weight and her pulse-rate had decreased in the same proportion as had her metabolism. Nevertheless, in view of the metabolism findings, I think we cannot but feel that she still has some thyrotoxicosis.

The next case is that of Miss M. T. P. (Laboratory No. 99, Hospital No. 211,454, W. M., W. S.). This patient, a woman of thirty-six years, I first saw on November 3, 1916. She had at that time had a goiter for eleven years and she had had symptoms of thyrotoxicosis for one year—marked nervousness, palpitation, and dyspnea. She had had prominent eyes for nine years, but nevertheless I could get no history of symptoms suggesting hyperthyroidism of longer duration than one year. She had lost 20 pounds at the time I saw her. Before coming under my observation she had had eight *x*-ray treatments apparently

without any definite improvement. On physical examination she showed extreme exophthalmos, very marked fine tremor of the fingers, and a thyroid gland considerably and asymmetrically enlarged, rather firm, and with a loud bruit. Her heart was definitely hypertrophied and showed a loud blowing systolic murmur at the apex transmitted to the axilla. The electrocardiogram gave evidence of left ventricular hypertrophy. The previous *x*-ray treatments were given at the Brigham Hospital,

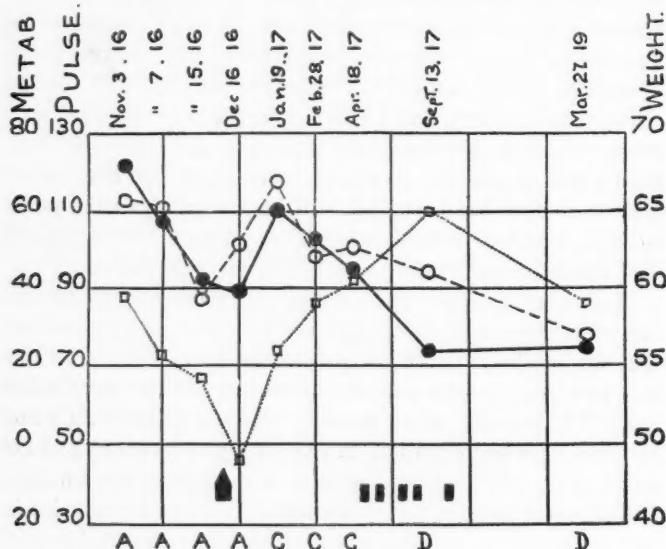


Fig. 218.—Miss M. T. P.

Boston, and upon her failure to improve they had advised operation, but she had refused.

At the Massachusetts General Hospital she was put to bed, and on November 15, 1916 her metabolism had dropped from plus 72 to plus 42 per cent. and her pulse from 112 to 89. It was felt, however, that she could only be cured by operation, and, accordingly, on November 23, 1916 Dr. Charles A. Porter excised the right lobe of the thyroid under gas and oxygen.

The pathologic examination of the removed tissue showed that many of the follicles were irregular and filled with granular colloid. They had a high columnar epithelial lining. There was no very definite papillary ingrowth. There were numerous focal areas of round-cell infiltration with occasional definite lymph-follicles. There were also wide bands of stroma running between the lobules. The anatomic diagnosis was struma parenchymatosa.

The patient made a good operative recovery, but nevertheless she lost weight rapidly after operation, and subsequently had an increase in basal metabolism to plus 60 per cent. on January 19, 1917, and a rise of pulse to 119. She then went along resting more or less at home and with no very definite improvement until April 18, 1917, when her metabolism was plus 46 per cent. It was then decided to give her further  $\alpha$ -ray treatment. On September 13, 1917 she had had four treatments and her metabolism had dropped to plus 24 per cent. I did not see her then for a year and a half, when, on March 27, 1919, she came in again for observation. She said that she had felt very much better during the last year and that she had been working to full capacity for a year and a half. Her work consisted in checking coats and hats in the cloak room of one of the large hotels in Boston. She was in good spirits and felt that she was on the road to recovery. Her metabolism was still plus 25 per cent., and she weighed less than when seen on September 13, 1917. Her eyes were still somewhat prominent, though less so than previously, and there was slight fulness of the left lobe of the thyroid, with a moderate bruit, but she had no tremor or other signs of hyperthyroidism.

This patient is to be regarded as a severe case of Graves' disease, probably of the vagotonic type, in whom a vigorous course of  $\alpha$ -ray treatment had accomplished but little, but who stood operation very well, and who later improved sufficiently to resume her normal life after five subsequent  $\alpha$ -ray treatments.

My last chart will be that of Mr. E. T. B. (Laboratory No. 137, Hospital No. 213,101, E. M., W. S.). This patient, a man

of thirty-five years, gave a history of having had some nervousness for six years and for four years had noted that his eyes were becoming prominent. I saw him first on February 3, 1917. He had been working up until that time. He had noted no increase in sweating and no diarrhea, but he did get short of breath on exertion. He said that his symptoms were worse three years ago, and then subsequently got better, and that for the last three weeks they had again returned in a more severe form than

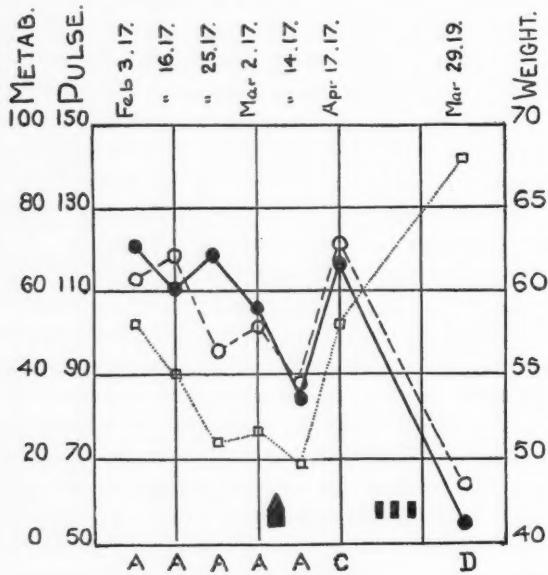


Fig. 219.—Mr. E. T. B.

he had ever had them before. On physical examination he showed slight exophthalmos, moderate tremor, and a thyroid gland moderately and symmetrically enlarged. It was soft and there was a faint bruit over both lobes. He too was of the vagotonic type, having a relatively high metabolism and not particularly high pulse, as a glance at his chart will show.

He was given nothing but rest in bed for about a month, and during that time he developed a very interesting complica-

tion. On February 11, 1917 he suddenly developed a temperature of 104° F., which apparently was due to a throat infection. Two days later his heart suddenly began to fibrillate. The electrocardiogram showed auricular fibrillation with rapid ventricular rate, and the *T* wave in Lead II was inverted. An electrocardiogram taken previous to this, on February 5th, had shown merely sino-auricular tachycardia, inverted *T* wave in Lead II, and a long *P-R* interval. He was given 69 grains of digitalis in the course of nine days, with satisfactory slowing in the pulse-rate, but the fibrillation continued.

It is interesting to note that the first metabolism observation, that of February 3d, was before he began to fibrillate, while those of February 16th and 25th and that of March 2d were during his fibrillation. Nevertheless, his metabolism continued to fall, and his condition was so satisfactory that in spite of the fibrillation he was transferred to the surgical side, and on March 5, 1917, an excision of the right lobe and isthmus was done by Dr. Charles A. Porter under novocain. The pathologic examination of the removed tissue showed great abundance of small irregular shaped follicles with wide bands of stroma running between them. There was a great deal of papillary infolding and a high, deeply staining epithelium. The anatomic diagnosis was follicular hyperplasia (toxic type).

He stood the operation well and showed a definite drop in metabolism afterward, but on April 17, 1917, after he had returned home, his pulse and metabolism had both risen again nearly to the point from which they started.

He was lost sight of then for nearly two years, but on March 29, 1919 he came in for observation. He told me that he had felt perfectly well and that he had been working for nearly two years. He had had three *x*-ray treatments following his operation. He still had slight exophthalmos, but had no signs or symptoms of thyrotoxicosis. His metabolism and pulse had both dropped to within normal limits and he had gained a great deal of weight; in fact, he was almost obese.

This patient is an example of the vagotonic type who was apparently cured by surgery followed by *x*-ray treatment.

Before closing I should like to discuss with you briefly 2 cases that died following operation, and to point out certain features about the metabolism which I think may be guides in selecting favorable from unfavorable surgical risks.

In the first place let us consider the case of Mrs. S. I. R. (Laboratory No. 77, Hospital No. 210,686, W. M., W. S.). This patient, a woman of twenty-nine years, gave a history of having had some fulness in her neck for two and a half years. She had also gradually developed nervousness and irritability, which were of an extreme type, but she had not noted any palpitation or dyspnea, nor had she had any increased sweating or appetite. For five or six months previous to her entry into the hospital she had had considerable diarrhea. She presented on examination the typical picture of very severe exophthalmic goiter—a moderate soft symmetric enlargement of the thyroid gland, with loud bruit, well-marked tremor, and slight exophthalmos. Her metabolism was first determined on September 26, 1916, when it was found to be plus 48 per cent. Her pulse at that time was 151.

On October 7, 1916, having rested in bed in the hospital in the interim, her metabolism was plus 47 per cent. and her pulse-rate 133. She had lost  $3\frac{1}{2}$  kg. in body weight since the previous observation. On October 21, 1916 her metabolism had risen to plus 58 per cent. and she had lost another kilogram of body weight. Her pulse, however, was slightly slower, being 124. The point I should like to emphasize is that her metabolism was rising in spite of her complete rest in bed, and although her pulse was falling slowly she was rather rapidly losing weight, and in all probability was becoming steadily more toxic. It was decided that her best chance lay in surgery, and so, on November 3, 1916, Dr. Charles A. Porter excised the entire right lobe and two-thirds of the left lobe, starting under novocain, but later using gas and oxygen. Pathologic examination of the excised tissue showed considerable variation in the size of the follicles, many of them being irregular and filled with a granular, shreddy colloid, while others contained little or no colloid. The epi-

thelium was frequently high and showed numerous papillary infoldings. There was a definite increase in stroma and there were many areas of lymphoid infiltration. The anatomic diagnosis was follicular hyperplasia. She did not stand the operation well and gradually grew more toxic, and died on November 5, 1916.

The interesting thing about this case is that, while her metabolism was only moderately elevated, which would lead us to suppose that she would stand operation well, she nevertheless had what we later found to be apparently a contraindication to operation, namely, a metabolism level rising in spite of complete rest in bed. I have seen the same thing in several other cases. The metabolism in the usual case shows a definite drop when the patient is put to bed. This drop usually continues for a matter of two to three weeks, when a level or plateau is reached, and beyond this plateau further drop will not occur through rest alone. The cases who when put to bed have a metabolism level which rises, should, to my mind, be regarded as very unfavorable ones for surgery.

My last case is perhaps the most interesting of the whole series, Mrs. F. G. (Laboratory No. 23, Hospital No. 201,801, E. M., W. S.). This patient, a woman of twenty-nine years, gave a history of having had an enlarged thyroid for the past eight years. She had noted that her eyes were prominent for seven years, and she had apparently had periods of thyrotoxicosis off and on over the same period. There had been several severe exacerbations followed by periods of apparent freedom from symptoms. The last exacerbation had lasted for nine months and she was gradually getting worse when seen. She had lost some 35 pounds, had intense nervousness, palpitation, and some dyspnea on exertion. She had considerable headache and paresthesiae of one sort or another. Her mental state was bordering on that of melancholia. She had had many severe attacks of diarrhea over a period of seven years, and this seemed to be one of the most conspicuous features of the case. On physical examination, she showed extreme emaciation, extreme exoph-

thalmos, and a thyroid gland markedly enlarged, hard, pulsating, and with a loud bruit. There was a well-marked fine tremor of the hands. A most interesting feature was a general bronze pigmentation of the skin. This was most marked in the lower abdomen, about the umbilicus, genitalia, and nipples, and least marked on the face. The heart showed a rough systolic murmur at the apex and a forcible impulse; in other respects it was not remarkable. Her blood-pressure was 130 systolic, 70 diastolic. Her white count was 7600 and there were 45 per cent. neutrophils, 44 per cent. small lymphocytes, 9 per cent. large lymphocytes, 1 per cent. transitional cells, and 1 per cent. eosinophils. Her urine never showed any sugar and only once a slight trace of albumin.

Only a single observation of the basal metabolism was secured. This was on May 24, 1915, when it was found to be plus 81 per cent. and her pulse-rate 121. It was felt then that her only hope of recovery was through immediate operation, but it was realized that she was a very poor surgical risk. On January 11, 1915 the left superior thyroid artery was ligated under novocain. She stood this fairly well and made a reasonably satisfactory recovery, so that on January 22, 1915 the right superior thyroid artery was ligated under gas and oxygen. The patient stopped breathing on the operating-table, but was finally revived and gotten back to the ward. Her condition was very bad—very rapid, thready pulse, stertorous breathing, and marked cyanosis. She was in a stuporous condition and remained so until her death on January 24th. The autopsy showed a purulent pericarditis and pleuritis, and also a condition of *status lymphaticus*.

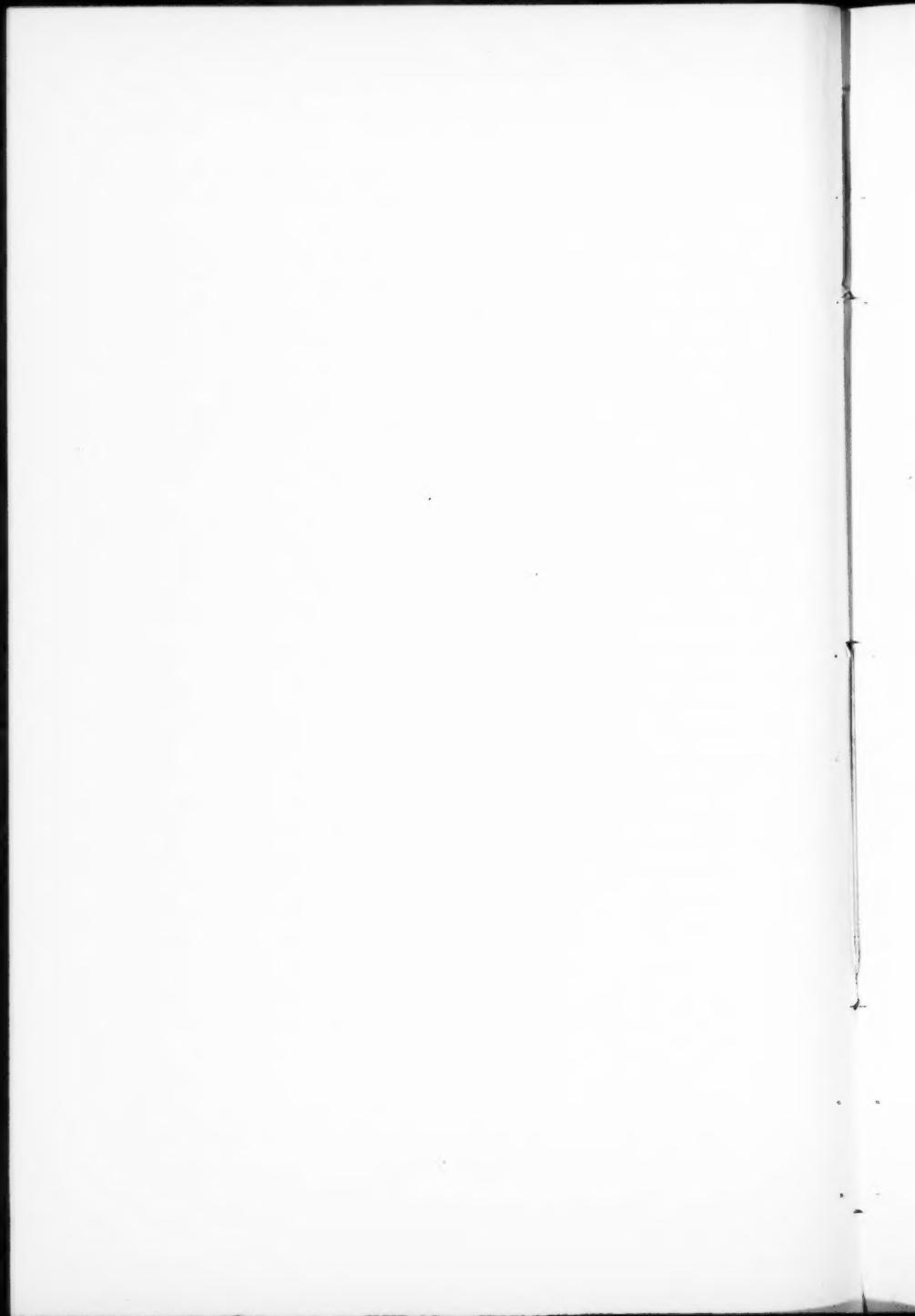
It seems fair to suppose that this patient died a thymic death. Her stormy symptoms before death are such as one sees in *status lymphaticus*, and at autopsy this condition was found. According to our present knowledge we certainly should not have advised operation in this case. Had she been given a course of *x-ray* treatments over her thyroid and thymus glands it is conceivable that the thymus could have been sufficiently involuted to make operation at a later date a safe procedure.

The chief points which I have tried to illustrate by this series of cases, and which I should like to refresh in your minds before closing, are as follows:

In the differential diagnosis of mild or atypical hyperthyroidism the determination of the basal metabolism furnishes a reliable guide. For example, it may be difficult to distinguish between, let us say, a case of effort syndrome and a case of mild hyperthyroidism, but the metabolism level is normal in the former and elevated in the latter, and so gives us the correct diagnosis. So, too, in a patient with an enlarged thyroid, but with slight or atypical symptoms of thyrotoxicosis, a metabolism determination tells us whether we are dealing with a toxic or non-toxic goiter.

In the matter of frank toxic goiter I hope that the charts of my patients have made clear that the essential factors that we must have to intelligently follow the progress and severity of the disease and the effects of treatment are the metabolism level, the pulse-rate, and the body weight.

Blood-sugar curves, adrenalin tests, and differential blood counts are instructive, but the metabolism level, to my mind, is essential. At the Massachusetts General Hospital we are now making the metabolism determination a routine test. It is no longer regarded as research, but as a part of the regular program in the management of Graves' disease. All frank cases are observed once or twice or more times before treatment is begun, then at regular intervals thereafter until recovery or death. From the behavior of the metabolism in the preliminary rest period we often draw our conclusion as to what form of treatment to use. With patients whose metabolism rises in spite of complete rest in bed we feel that surgery is very dangerous. With the type of case with greater rise in metabolism than in pulse we feel that *x*-ray of the thymus and thyroid should precede surgery, to avoid the possibility of a thymic death. My own feeling is that our results have shown that it is always wise to employ the *x*-ray first in any event, with the idea that the chances are good that it alone may cure, and that, if not, it will reduce the risk of subsequent surgery.



## CLINIC OF DR. REGINALD FITZ

MASSACHUSETTS GENERAL HOSPITAL

### SURGICAL ANESTHETICS IN DIABETES MELLITUS

#### The Dangers of Operative Treatment When Necessary in Diabetic Patients; Necessity, if Possible, of Pre-operative Treatment in Diabetics; Importance and Relative Merits of Methods of Anesthesia Adopted in These Cases; Illustrative Cases.

DR. JOSLIN<sup>1</sup> has pointed out in his text-book on the Treatment of Diabetes Mellitus the well-known fact that diabetic patients with surgical complications may stand in need of operation more than do normal individuals or those suffering from most other chronic diseases, but are exposed to certain operative risks which non-diabetic cases largely escape. Today I propose to emphasize the force of Dr. Joslin's statement and to illustrate the possible dangers following the use of anesthetics in this disease.

TABLE I

Year.	Total number of diabetic patients admitted.	Diabetic patients admitted with surgical complications.	Percentage of diabetic patients with surgical complications.
1913.....	34	8	23
1914.....	53	16	30
1915.....	87	10	12
1916.....	115	16	14
1917.....	97	4	4
Total.....	386	54	
Average.....	77	11	14

Table I shows the total number of unquestioned diabetics admitted to the Massachusetts General Hospital during a

period of five years, and, of these, the number admitted as surgical cases. The five-year period preceding 1918 was selected as being uninfluenced by the abnormal conditions of the war, and is probably fairly typical of any five years in the recent history of the institution.

As can be seen, about 14 per cent. of the 386 diabetics admitted had symptoms which made the judgment of a surgeon as urgently needed in the treatment of the case as that of a medical man. This fact at once justifies the assertion that diabetes is by no means a medical disease exclusively. Surgical conditions complicating it are relatively common. A surgeon must, therefore, know the life-history of the disease in order to balance the risks of operation in a given case, and if operation is necessary, he must be thoroughly familiar with the effect of different anesthetics and operations upon diabetics in order to expose his patient to as little danger as possible.

In this series 9 of the 54 cases with surgical complications were obviously unsuited for operation either because of the patient's general health or because the surgical condition which presented did not warrant operative interference. These cases will not be considered any further; 45 cases came to operation, however, and the results are summarized in Table II.

There were 13 deaths in this series of surgical cases, or a total mortality of nearly 30 per cent., a figure which illustrates the well-known teaching that diabetics do not stand operation easily. However, on closer analysis the cases may be logically subdivided into two groups, the first consisting of 20 cases which were suffering from an acute infection or gangrene before operation, and the second consisting of 25 non-infected cases. Since 10 of the infected cases died (50 per cent.) and only 3 of the non-infected cases (12 per cent.) it becomes clear that any acutely infectious condition in a diabetic requiring surgical interference must be at once considered of utmost gravity, while any non-infectious condition requiring operation is more dangerous than normal, but can be safely carried through.

The majority of the patients were old people, and therefore, probably, mild cases. Only 3 individuals under thirty years of

age were operated upon. Two of these died, and the one which recovered had so few diabetic signs and symptoms as to justify the query whether he actually had true diabetes. These figures are therefore significant. The more severe the diabetes, the greater is the risk of operation.

Local anesthesia was used in 12 cases, spinal anesthesia in 8 cases, gas-oxygen anesthesia in 11 cases, and ether anesthesia in 14 cases; 3 of the fatal infected cases were given local anesthesia, 5 were given spinal anesthesia, 4 were given gas-oxygen anesthesia, and 1 was given ether anesthesia. There seems no reason for assuming, in the infected cases at least, that one anesthetic was more harmful than another. In the non-infected group, on the other hand, there were no deaths after local or gas-oxygen anesthesia, while 1 patient died after spinal anesthesia and 2 after receiving ether.

The majority of the infected cases were surgical emergencies and could not receive a thorough course of preoperative treatment; 4 cases, however, were thoroughly prepared for operation by a prolonged course of medical treatment; 2 died, both being patients under thirty years of age; 2 others were aglycosuric just before operation, but both died. The remaining 14 cases were operated upon soon after entering the hospital and suffered a mortality of 6, or 43 per cent. How important preparation is for operation in a septic case is, therefore, an open question, as judged from these figures. The prolonged undernourishment necessary to get a patient's urine sugar and acid free and to get his blood-sugar, fat, and acetone body concentration normal may so lower his resistance to infection as to be unjustifiable. The best rule would seem to be to postpone operation as long as seems safe as judged by the clinical condition of the patient, but not to wait until septicemia has developed, or until the patient is so weak that his powers of recuperation and resistance are lost.

Nine of the 25 non-infected cases in which there was ample time for preoperative preparation were given prolonged medical treatment, and were turned over to the surgeons after sufficient observation. Of these 9, none died, although 4 were given

TABLE II<sup>1</sup>

Num-ber.	Age.	Surgical condition.	Operation.	Anesthetic.	Result.
1	38	Carbuncle	Excision	Local	Death in coma
2	75	Infection of neck	Incision and drainage	Local	Death in coma
3	50	Cellulitis of neck	Incision and drainage	Local	Death in coma
4	60	Gangrene of leg	Amputation	Spinal	Death ten days later of embolus
5	65	Appendicitis	Appendectomy	Spinal	Death from embolus
6	63	Inguinal hernia	Radical cure	Spinal	Death in coma
7	62	Carbuncle	Excision	Gas-oxygen	Death from septicemia
8	23	Acute appendicitis	Appendectomy with drainage	Gas-oxygen	Death in coma
9	54	Cellulitis of arm	Incision and drainage	Gas-oxygen	Death from septicemia and possibly coma
10	30	Pyonephrosis	Nephrectomy	Gas-oxygen	Death from peritonitis
11	52	Acute appendicitis	Appendectomy	Ether	Death from embolus
12	54	Hernia in scar	Radical cure	Ether	Death in coma
13	67	Cancer of the uterus	Hysterectomy	Ether	Death in coma
14	53	Carbuncle	Partial excision and drainage	Local	Relieved
15	43	Abscess of back	Incision and drainage	Local	Relieved
16	42	Cellulitis of axilla	Incision and drainage	Local	Relieved
17	61	Fistula in ano	Excision	Local	Relieved
18	49	Hydrocele	Radical cure	Local	Relieved
19	49	Femoral hernia	Radical cure	Local	Relieved
20	48	Lipoma, multiple	Excision	Local	Relieved
21	36	Hemorrhoids	Ligation of hemorrhoids	Local	Relieved
22	48	Varicose veins	Dissection	Local	Relieved
23	61	Gangrene of foot	Amputation	Spinal	Relieved

24	53	Umbilical hernia	Radical cure	Spinal
25	57	Lacerated perineal sphincter	Perineorrhaphy	Spinal
26	52	Incompetent vesical sphincter	Plastic on bladder	Spinal
27	43	Lacerated perineum	Perineorrhaphy	Spinal
28	53	Septic hand	Incision and drainage	Gas-oxygen
29	53	Septic hand	Incision and drainage	Gas-oxygen
30	62	Carbuncle of neck	Incision and drainage	Gas-oxygen
31	56	Carbuncle of neck	Incision and drainage	Gas-oxygen
32	62	Septic foot	Incision and drainage	Gas-oxygen
33	41	Fistula in ano	Excision	Gas-oxygen
34	51	Subdeltoid bursitis	Manipulation	Gas-oxygen
35 <sup>a</sup>	27	Acute cholecystitis	Cholecystectomy	Ether
36	45	Hernia in scar	Radical cure	Ether
37	60	Cholelithiasis	Cholecystectomy	Ether
38	44	Cancer of the breast	Excision	Ether
39	57	Cystocele	Colporrhaphy	Ether
40	65	Cancer of the breast	Excision	Ether
41	40	Chronic metritis	Hysterectomy	Ether
42	54	Duodenal ulcer	Gastro-enterostomy	Ether
43	46	Endometritis	Curettage	Ether
44	66	Parotid tumor	Excision	Ether
45	57	Cystocele	Colporrhaphy	Ether

<sup>1</sup> These cases are not in chronologic order.

<sup>a</sup> This case clinically was so mild as not to be a proved diabetic.

ether and 2 were given spinal anesthesia. Two were made glycosuric just before operation, but were not given any prolonged treatment. One died following ether anesthesia and 1 lived following spinal anesthesia; 14 were directly admitted to surgical wards and were operated upon without consideration of the diabetes; 2 died, 1 after ether anesthesia and 1 after spinal anesthesia; 6 others were given ether with impunity. 1 was given spinal anesthesia; 1 was given gas-oxygen, and 4 were given local anesthesia.

Certain conclusions are justified from this brief statistical survey. It is evident that no diabetic is as good a surgical risk as is a normal individual. No diabetic with an acutely infectious process is as good a surgical risk as one without signs of infection. A prolonged course of preoperative treatment whenever possible is essential to minimize the dangers of operation in a diabetic. The risk of any operation for a properly prepared non-infected diabetic case is slight, but local anesthesia or gas-oxygen are safer anesthetics than spinal anesthesia or ether.

As I wish to emphasize the possible dangers following the use of anesthetics in diabetes mellitus I shall discuss in detail 4 cases which were recently operated upon in the Massachusetts General Hospital and which were carefully studied in order to inquire into the immediate effect upon the diabetic individual of local, gas-oxygen, spinal, and ether anesthesias.

**CASE I.**—No. 231,871, an Italian girl, twenty-one years old and single, entered the hospital on July 28, 1919. The essential features of her history were that she began to feel ill a year previously, loosing weight rapidly, and always being hungry and thirsty. About nine months before entry she developed a perirectal abscess, which discharged pus intermittently but never healed. Since the onset of her illness she had lost about 34 pounds in weight.

Routine physical examination was negative except that there was marked induration around the rectum, with redness, swelling, and tenderness on the left side, which suggested a large abscess.

The urine contained much sugar and gave a heavy ferric chlorid reaction.

The mouth temperature at entry was 101° F., the pulse-rate 120, and the respiration rate 40.

It was considered advisable to drain the abscess immediately under local anesthesia. The effect on blood and urine is shown in Table III.

As can be seen by this table, the patient at entry was in a serious condition from a diabetic standard. Her blood was so rich in fat as to appear creamy, there was a high blood-sugar concentration, the acetone body concentration was much increased, and there was a coexistent severe acidosis as measured by Van Slyke's method. The urine, confirming the blood-picture, showed a great deal of sugar and a high excretion of acetone bodies.

The operation, of course, amounted to nothing. However, the case is shown to demonstrate that the injection of a local anesthetic, even in a case with severe acidosis, was not accompanied by any harmful results. On the following day the blood-fat concentration was less, the blood-sugar was slightly lowered, there was considerably less blood-acetone concentration, and the acidosis, as measured by Van Slyke's method, was improved.

A word should be said about the dietetic treatment. The patient was urged to drink plenty of fluid. She was not fasted at the outset, but was given a diet low in fat (on account of the acidosis and increased blood-fat concentration) with considerable protein and carbohydrate. As this diet seemed to be effective, it was not changed.

The subsequent course was uneventful. The patient's condition improved. The abscess healed quickly. The temperature, pulse, and respirations became normal. An unexplained finding is that of the increased acetone body excretion on the day following operation.

The increase in blood-sugar concentration and excretion of sugar in the urine due to stolen food were incidental to the operation, and did no immediate harm to the patient.

On the whole, then, this case demonstrates that local anes-

TABLE III

Date, 1919.	URINE.			BLOOD.			DIET.			REMARKS.		
	Volume, c.c.	Nitrogen, g.m.	Total acetone, g.m.	Sugar, g.m.	Fat, per cent.	Total acetone, mgm. per 100 c.c.	Plasma combining power per 100 vols., per cent.	Fat, g.m.	Carbohydrate, g.m.			
July 28	2700	9.2	57.0	8.3	2.6	.29 <sup>a</sup>	76.4	.28	50	11	75	614
29	3100	...	51.6	12.2	2.1	.28	56.2	36.6	50	11	75	614
30	2700	9.6	37.5	7.2	...	...	...	...	50	11	75	614
31	4400	14.1	59.5	9.2	1.5	.38	52.4	35.3	50	11	75	614
August 1	3300	16.5	53.2	3.5	...	...	...	...	50	11	75	614
	...	...	...	...	...	...	...	...	50	11	75	614
	2	...	...	...	...	...	...	...	50	11	75	614

<sup>1</sup> In this and the following tables "total acetone" in blood or urine includes the acetone derived from acetone, diacetic acid, and beta-hydroxybutyric acid, the whole expressed as acetone.

<sup>2</sup> Blood taken before operation.

thesia for a mild operation, even in the presence of infection, may be given without harm to a diabetic with pronounced acidosis, hyperglycemia, hyperlipemia, and hyperacetonemia.

CASE II.—No. 232,817, an Italian male laborer, fifty-seven years old and married, entered the hospital on September 22, 1919. His past history was unimportant except that about twenty years previously his urine was examined by a doctor and "showed a little trouble." A diet was prescribed which excluded white bread and all food which contained sugar. The patient followed this diet for about six months, and after that time ate everything.

A year before entry he suffered from an attack of influenza and was in bed for three weeks. He made a normal recovery, but since then noticed that his appetite was enormous, despite which he lost weight rapidly. Following his influenza he weighed 185 pounds and now weighed, he thought, only 116 pounds.

Three weeks before entry he was suddenly seized with a sharp knife-like pain in the right chest at about the level of the shoulder-blade. The pain did not radiate. At first there was no cough, but it began about a week after onset of illness and was now very annoying and constant.

Physical examination was negative except for signs in the right chest, which suggested fluid. An x-ray plate showed that the right chest was contracted, and that the diaphragm on the right side was high and fixed. The heart was not displaced. There was an area of dulness extending across the right mid-chest to the axillary border.

The Wassermann reaction was negative. The white count varied between 15,000 and 34,000. The urine contained much sugar, but did not show a positive ferric chlorid reaction. The sputum, which was of varying amount, was foul and purulent and contained numerous different organisms and leukocytes, but no tubercle bacilli. While under observation on the medical ward the patient ran a septic temperature chart with a rapid feeble pulse, and with variable dyspnea.

It seemed probable that the patient had an encapsulated empyema complicating a diabetes. As he seemed to grow worse with such drainage as was possible through the bronchi, his chest was finally drained through the pleura under gas-oxygen anesthesia. The urine and blood findings in relation to this operation are given in Table IV.

As can be seen, the urine became free from sugar upon a restricted diet. There was no significant acidosis. The blood-sugar remained persistently high until the carbohydrate intake was reduced to 15 grams a day, and kept at such a low level for a week.

On October 14th, after the urine had been free from sugar for two weeks except for very small amounts upon two occasions, the blood-sugar concentration was .12 per cent., the blood-fat was .50 per cent., and the blood-acetone concentration was 13.7 mgm. per 100 c.c. Operation was decided upon, and in preparation the diet was not changed, but fluids were forced. On the following day (October 15th) the volume excreted was 3470 c.c. and the total acetone excreted was .87 gm. On the morning of operation (October 16th) the blood-sugar concentration was .15 per cent., the blood-fat was .65 per cent., the blood-acetone concentration was not changed, and there was a slight but definite acidosis, as shown by the lowered combining power for  $\text{CO}_2$  in the plasma.

The patient went through his operation satisfactorily. The immediate effect seemed to diminish the output of fluid, to produce glycosuria, and to increase the excretion of acetone bodies. The blood analyzed on the morning after operation showed that the blood-sugar concentration had increased, but that the blood-fat concentration had diminished. Another interesting observation was the apparent reaction of the acetone bodies. The total acetone bodies in the blood were significantly lower than before operation and the plasma's combining power for  $\text{CO}_2$  was increased, suggesting that such mild acidosis as had been present before operation had cleared up. One conclusion is justified in this case. Gas-oxygen anesthesia, although apparently accompanied by hyperglycemia, glycosuria, and in-

TABLE IV

Date.	URINE.			BLOOD.			DIET.			REMARKS.
	VOLUME.	NITROGEN, gm.	GLUCOSE, gm.	TOTAL ACETONE, gm.	GLUCOSE, gm.	TOTAL ACETONE, gm.	PROTEIN, gm.	FAT, gm.	CARBOHYDRATE, gm.	
1919.	Sept. 23	3160	37.3	98.4	Traces	.61	.37	50	50	875
	24	1470	20.5	49.0	Traces	...	...	50	50	875
	26	1750	14.1	17.5	Traces	...	...	50	50	875
	28	1900	10.4	Neg.	...	...	...	...	...	
Oct. 1	2200	15.2	Trace	Traces	.57	.16	10.6	...	50	29
	5	1100	11.5	Neg.	...	...	...	...	50	29
	7	960	7.0	Neg.	Traces	.42	.20	10.0	...	50
	9	1350	11.2	Trace	Traces	...	...	...	...	29
	11	760	...	Neg.	Traces	...	...	...	...	15
	13	640	7.4	Neg.	Traces	...	...	...	...	60
	14	1820	...	Neg.	...	.50	.12	13.7	...	48
	15	3470	12.5	Neg.	.87	...	...	...	...	15
	16	1090	5.9	10.9	2.27	.65	.15	15.6	52.0	...
	17	2740	6.7	Trace	.49	.56	.24	6.1	68.0	3
	15	1520	...	Neg.	...	...	...	...	...	21
	19	3000	9.1	Neg.	.93	.68	.18	14.5	68.0	40
	20	900	6.8	Neg.	.50	...	...	...	...	27
						...	...	...	...	20

<sup>1</sup> Blood taken before operation.

creased excretion of acetone bodies, was not accompanied by signs of acidosis in the blood. It is possible that the pure carbohydrate diet given on the day of operation played a part in these findings. On the other hand, it is possible that the administration of oxygen made it easier for the body to burn acetone bodies, and thus acidosis was actually prevented. Further observations are necessary to explain more thoroughly what happened.

After operation the patient made an uneventful recovery and was able a few days later to take 1500 calories, 70 grams of protein, and 20 grams of carbohydrate without glycosuria or significant acidosis.

On the whole, this case is demonstrated to show that while gas-oxygen anesthesia may produce hyperglycemia and glycosuria in a diabetic, it does not necessarily cause acidosis. It is perhaps on this account that gas-oxygen anesthesia is a better anesthetic for diabetics, according to the statistics, than spinal anesthesia or ether.

**CASE III.**—No. 232,779, a man forty years old, married, and engaged in the laundry business, entered the hospital on September 20, 1919 for a hernia which he had had for sixteen years. His history was negative except for influenza ten months previously, following which he had noticed that he urinated twice at night, but had no accompanying symptoms of increased appetite or thirst. Two years before entry, however, he weighed 196 pounds, and now about 145. This loss of weight had been gradual, but had been more marked during the ten months following his influenza attack.

Routine physical examination was negative except for a large left inguinal hernia. The urine contained a faint trace of sugar, the blood-sugar concentration at entry was .28 per cent., the blood-fat concentration was .63 per cent., and there was no evidence of acidosis, the blood-acetone concentration being less than 10 milligrams per 100 c.c. of blood. Slight restriction in diet caused the glycosuria to disappear and the blood-sugar concentration to drop to .12 per cent. The blood-fat and blood-acetone concentration remained unchanged. The case, there-

fore, appeared to be one of mild diabetes accompanied by a large inguinal hernia which the patient was anxious to have cured. An operation was performed under spinal anesthesia. The apparent effect of this anesthetic upon the diabetes is shown in Table V.

On the morning of operation the urine was sugar free, the blood-sugar concentration was .10 per cent., the blood-fat concentration was .57 per cent., and the blood-acetone concentration was 38 milligrams per 100 c.c. of blood. The last figure was abnormally high and might have suggested that the patient was prone to develop acidosis, as the increase came on after a partial fast day when the only food eaten was carbohydrate and protein. Despite this danger sign, the operation was performed, and the immediate results were striking. No sugar appeared in the urine on the day of operation. However, a very heavy ferric chlorid reaction developed in the urine at once and the total acetone excretion for twenty-four hours rose from 1.9 to 15.6 grams. The blood taken on the morning after operation showed that the blood-sugar concentration had doubled, the blood-fat concentration had increased, and the blood-acetone concentration had risen to 50.2 milligrams per 100 c.c. blood. Unfortunately, the actual degree of acidosis as shown by the combining power of the plasma for  $\text{CO}_2$  was not estimated. However, the patient himself noticed his own deep breathing and air hunger and felt stupid and miserable. Fluids were forced, a pure carbohydrate diet was given, and the acute acidosis disappeared as suddenly as it began. Traces of sugar appeared in the urine for two days, but then cleared up. The excretion of acetone bodies diminished rapidly. The blood-sugar concentration in the blood dropped slowly but consistently toward normal, the blood-fat concentration fell more quickly to its preoperative level, and the blood-acetone bodies diminished with remarkable rapidity.

On the whole, this case is shown as a mild diabetic who was given spinal anesthesia. Apparently the immediate effect of this procedure was to cause hyperglycemia, hyperlipemia, and so severe an acidosis as to suggest impending coma. Why such

TABLE V

Date.	Urine.		Blood.		Dirt.		REMARKS.
	V <sub>o</sub> lume.	Nitrogen, gm.	Sugar, gm.	Nitrogen, gm.	Protein, gm.	Carbohydrate, gm.	
September 1919.	1750	7.7	Neg.	Less than 1.00	.12	.63	Less than 10.0
	1500	8.7	Neg.	Less than 1.00	....	....	70
	28	2500	6.2	Neg.	1.90	.... <sup>1</sup>	....
	29	1300	4.0	Neg.	15.60	.10	....
	30	1030	7.3	Trace	5.15	.20	....
	October 1	2600	9.4	Trace	1.00	....	....
2	3250	13.5	Neg.	Less than 1.00	.17	.57	....
3	680	7.3	Neg.	Less than 1.00	....	....	....
4	1740	14.3	Neg.	1.00	.16	.51	....
					Less than 10.0	10.0	57
						60	25
							875

<sup>1</sup> Blood taken before operation.

a result should have occurred is not explained, as the subject demands further and more complete study. If, however, such a reaction is typical of the effect of spinal anesthesia upon a mild diabetic patient, it at least suggests why this method of anesthesia has been fatal in the case of patients who were more severely diabetic and who were not carefully prepared for operation, and why it may be the most dangerous of the three anesthetics which have been so far discussed.

**CASE IV.**—No. 231,511, a Jewish woman forty years old, entered the hospital on July 5, 1919, complaining of pain in her left side. Her previous history was unimportant except for her statement that she "had heart trouble seventeen or eighteen years ago" and since had noticed palpitation of her heart on exertion accompanied at times by swelling of her ankles and feet.

She had been married seventeen years, never became pregnant, and had always suffered from painful menstruation. For several years she had noticed almost constant pain in her left side, which had gradually become so severe that she now felt thoroughly discouraged and worn out.

She was unable to give any statement in regard to loss of weight. She had noticed nothing remarkable about her digestive or urinary systems except that her bowels were constipated and for the last three or four years she had been getting up twice at night to urinate. Her chief complaint was referable to the pain in her side and her other symptoms seemed negligible.

Routine physical examination of her heart, lungs, abdomen, and extremities was negative except for a slight general arteriosclerosis with blood-pressure increased to 166 mm., and for a mass about the size of an orange above the symphysis. Pelvic examination revealed a retroverted uterus with a soft cervix which bled easily and which felt abnormally hard on the upper surface. The mass above the symphysis was anterior to the cervix and apparently connected with the uterus. The urine contained a trace of sugar.

The diagnosis was made of a uterine fibroid complicating a

mild diabetes. On account of the long-standing history it seemed best to advise operation.

The patient was given ordinary diet without bread or sugar for four days. The urine showed a trace of sugar each day and gave a negative ferric chlorid reaction.

On July 10th the blood and urine findings were as follows:

URINE.				BLOOD.			
Volume.	Nitrogen, gm.	Sugar, gm.	Total acetone bodies, gm.	Sugar, per cent.	Fat, per cent.	Total acetone bodies mgm. per 100 c.c.	
1420	8.2	2.7	Less than 1.0	.34	.68	Less than 10.0	

The blood-sugar concentration was abnormally great, although there was only a slight sugar excretion in the urine after a very liberal diet. There was no evidence of acidosis, the blood-fat concentration was within normal limits. It was reasoned from these facts that the diabetes was mild, and as the patient's general condition was so good, a hysterectomy was performed under ether anesthesia two days later (July 12th) without any preoperative diabetic treatment. The clinical and laboratory findings illustrating the effect of this anesthetic upon the patient are given in detail.

July 12th: Urine examined before operation was free from sugar and the ferric chlorid reaction was negative.

Blood-sugar before operation not determined.

Blood-fat before operation was 0.44 per cent.

Total blood-acetone bodies before operation less than 10 mgm. per 100 c.c.

Blood-pressure before operation, 148 mm. systolic, 100 mm. diastolic.

The patient was given, subcutaneously,  $\frac{1}{8}$  grain morphin and  $\frac{1}{20}$  grain atropin at 9 A. M. At 10 A. M. ether was started by the cone method. The patient became easily anesthetized, so that operation was begun at 10.16; 4 ounces of ether were used,

the cone being removed at 10.30 and the operation being completed at 11.00. The patient was conscious an hour later and in good condition. During anesthesia she did not struggle, her pulse and respiration were regular and not rapid. Following operation there was but slight shock, as shown by the blood-pressure, which dropped four hours after operation from 148/100 to 120/85, but returned to 148/95 within twenty-four hours.

The following observations were made upon the blood and urine after operation.

Hours after operation.	URINE.				BLOOD.		
	Volume, c.c.	Nitro- gen, gm.	Sugar, gm.	Total acetone bodies, gm.	Fat, per cent.	Sugar, per cent.	Total acetone bodies milligrams per 100 c.c.
5 hours	...	...	...	...	.95		
24 hours	480	3.1	15	1.4	...	.45	35.3
48 hours	1220	8.2	43	3.2	.70	.43	53.2
60 hours	Patient died.						

This table is very significant. As can be seen, within five hours after anesthesia the concentration of fat in the blood had doubled, within twenty-four hours the blood-sugar concentration had risen, and a rapid accumulation of acetone bodies had occurred in the blood; within forty-eight hours the blood-sugar concentration had not changed, but the blood-fat had diminished, and the blood-acetone bodies had increased to a greater extent. The urinary findings are equally important. During the first twenty-four hours after operation but little urine was excreted, and it contained small amounts of nitrogen, relatively large amounts of sugar, and enough acetone bodies to cause a heavy ferric chlorid reaction. During the second twenty-four hours after operation the volume of urine was increased, it contained large amounts of nitrogen and sugar, and showed a further increase in acetone body excretion. The patient died about sixty hours after operation, with a rapid pulse, rising temperature, and considerable dyspnea. Presumably she died of

acidosis, although the coexistent signs of diffuse bronchitis with fever suggest that she may have developed a terminal bronchopneumonia.

The probable explanation for the rapid development of the fatal acidosis in this case is found in the pharmacologic properties of ether.

Besides acting as an anesthetic, ether has an immediate and definite effect upon the body fats and upon the liver. Following the administration of ether to normal dogs, Bloor<sup>2</sup> was able to demonstrate a marked rise in the concentration of blood-fat apparently referable to the fact that there was an increased solubility of the fatty substances of the tissues in the blood-ether mixture. Sansum and Woodyatt<sup>3</sup> have shown that ether produces an immediate hyperglycemia in dogs made diabetic by phlorizin because it breaks down the liver glycogen under the stimulus of asphyxia and transforms it into sugar. Moreover, they have demonstrated in such animals that ether causes a temporary suppression in excretion of urine, nitrogen, glucose, and acetone bodies, with the result that there is little output of these substances for several hours. This patient correlates clinical findings with the facts observed in animal experiments. Here, as in animals, the blood-ether mixture seemed to dissolve a considerable amount of fat from the tissues and to cause a hyperlipemia. At the same time the ether appeared to break down glycogen in the liver into sugar, with resultant hyperglycemia, and finally, excretion was greatly diminished, so that there was a suppression for twenty-four hours of the excretion of sugar, acetone, and nitrogen. All these reactions together were sufficiently serious to upset the delicate equilibrium which the patient was forced to maintain in order to live, and death probably resulted from acidosis because when the fat so rapidly set free was reabsorbed from the blood into the tissues it was turned into acetone bodies because the carbohydrate necessary to burn it normally was not available, and because the conservative polyuria which helps to wash out these substances was lacking.

On the whole, this case is demonstrated in order to show that ether may be a fatal anesthetic for even an apparently mild

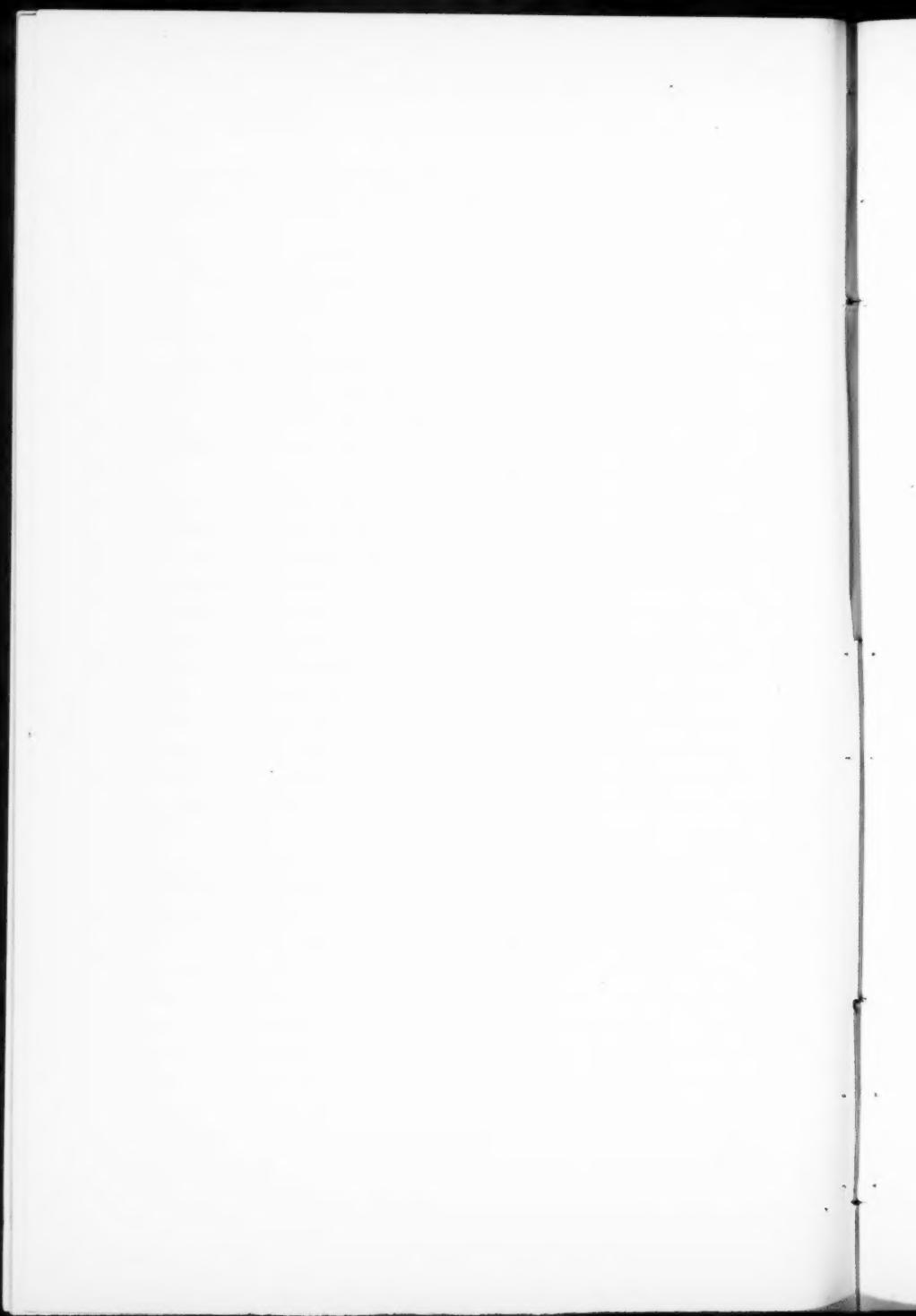
diabetic, and that on account of its pharmacologic activities its use is contraindicated as an anesthetic for any diabetics undergoing surgical operations.

In conclusion, I would emphasize the following points brought out in this clinic. The surgical complications of diabetes mellitus are so common that surgeons should become thoroughly familiar with the natural course of the disease. A diabetic with any infectious process requiring operative interference must be regarded as critically ill. A course of dietetic treatment in preparation for operation should be undertaken when possible, and should be insisted upon in all uninfected cases where the surgical complication is not an acute emergency.

The 4 cases discussed show that it is possible to study the immediate effects on the body as a whole of the anesthetics in common use, and that in diabetic patients these effects may be of important clinical significance. Further observations along these lines will determine better methods for preparing diabetic patients for operation, safer methods for administering anesthetics, and better methods for overcoming the immediate reactions to anesthetics. At the moment it is safe to say that of the anesthetics commonly used for diabetics local anesthesia is the safest for minor operations, gas-oxygen is the best for major operations, spinal anesthesia may prove dangerous, and ether, on account of its pharmacologic properties, is contraindicated.

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## CLINIC OF DR. FRITZ B. TALBOT

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### WHOOPING-COUGH

THE first distinct and comprehensive account we have of the disease was furnished by Maezray in the year 1414 in his chronologic history of France. The first epidemic of whooping-cough was described by DeBaillou in the sixteenth century. Since the seventeenth century it has been common in all latitudes. It may appear in epidemics in schools or any other gathering place of children, or a child with an undiagnosed case of whooping-cough may leave a long trail of the disease in its travels from one city to another.

It is a highly contagious and infectious disease, and is usually transmitted by direct or immediate contact. There is little doubt that infection is spread through the sputum, which is scattered by the coughing, although it is conceivable that the infection could be carried by the sputum adhering to the clothes of a third person. This method of spreading, however, is highly improbable. Nothing in my experience would support such an assumption, and I feel perfectly safe in going from one patient to another after washing the hands and taking the ordinary precautions. There is evidence that the virulence of the sputa is only short lived and that the infecting organism dies quickly.

There is a tendency for epidemics to occur more frequently during the winter and spring. The fact that there seemed to be a connection between epidemics of whooping-cough and measles caused early investigators to attempt to correlate the two diseases. This, however, could not be done. There is little doubt that the great frequency of the disease during the winter and spring months is due to the gathering of children in school and

in public conveyances in bad weather. In large cities there are always sporadic cases, but in rural communities, where social life resembles more the life of one big family, and where all the children of the community usually come more in contact with one another, an epidemic will sweep through the whole community of children, and will not appear again until a new group of children become exposed.

**Age Incidence.**—It is assumed that children are more susceptible than adults and that pertussis is a disease of childhood. It is probable, however, that if a virgin field were inoculated there would be as many adults as children affected. The majority of cases appear in the first ten years of life, with a stronger tendency to affect young infants than any other contagious disease. A number of cases have been reported during the first month of life while the infant was still on the breast. This is quite different from measles, which is rarely found in breast-fed babies. The largest proportion of cases occur during the first two years of life, but the age of compulsory school attendance is also greatly affected.

**Immunity.**—Recovery from one attack, as a rule, confers lifelong immunity. There have been instances, however, in which elderly people have had the disease a second time.

**Infectiousness.**—Pertussis is infectious from the beginning of the catarrhal stage and undoubtedly continues so throughout the first three weeks of the disease. It is probably more infectious during the catarrhal stage than at any other time during the disease.

**Bacteriology.**—The etiology of pertussis has been discussed for years. In 1906 Bordet and Gengou showed that the influenza-like bacillus found in the sputum of whooping-cough was a different organism from the one described by Pfeiffer as the cause of influenza. The morphologic characteristics of the two organisms are essentially the same and can only be differentiated in culture. Unlike the bacillus of whooping-cough, the influenza bacillus cannot be made to grow on a medium that does not contain hemoglobin.

**Incubation.**—The indefinite and uncertain onset of the dis-

ease makes it almost impossible to determine the period of incubation. Different writers vary on the time, the shortest being three days and the longest fifteen. It is generally believed that if sixteen days pass after exposure without symptoms, there is very little chance of the disease appearing. After three weeks expire without infection there is no chance of the child coming down with the disease.

**Symptoms.**—It is customary to divide the course of whooping-cough into three stages—the catarrhal, the spasmodic, and the stage of decline. The catarrhal stage commences with sneezing, more or less cough, and sometimes slight fever. This may last for about ten days, with individual variations, and is often accompanied by a temperature of  $99^{\circ}$  to  $100\frac{1}{2}^{\circ}$  F. This temperature usually disappears after two weeks' time. Some children whoop during the first week, while others go through the entire course of the disease without whooping. The cough at the beginning, although spasmodic, is often indistinguishable from the cough of ordinary bronchitis, and may not excite suspicion unless it is known that the patient has been exposed to pertussis. The progress of the disease differs from an ordinary cold in that the symptoms increase in severity.

In the spasmodic stage the cough becomes spasmodic and is more frequent during the night, gradually assuming the typical paroxysms of whooping-cough. The paroxysms of coughing may occur spontaneously or may be brought on by sneezing, swallowing solid morsels of food, running, or great anger. Older children are warned of an attack by tickling in the throat, choking, or a feeling of suffocation, which causes great anxiety. These symptoms cause the child to run to its mother, grasp a chair, or lean against the wall. A paroxysm may last from two to five minutes, and only cause slight interruption in the play of healthy children, while their weaker brothers are tired out and often wish to lie down or to be held by their parents. In young children vomiting is almost certain to follow the paroxysm. The daily number of paroxysms varies with the strength of the child and the severity of the disease. During the height

of the disease there may be as many as fifty paroxysms in twenty-four hours.

The convulsive stage is the height of the disease. There is a tendency for it to increase, remain at its height, and then decline. In recent epidemics here the disease has become progressively worse for three weeks and declined in three weeks, having a total course of six weeks. The duration of the convulsive stage cannot be easily fixed and is influenced by climate, surroundings, and the severity of the infection. There is a tendency for the course of the disease to be more prolonged and severe during the winter months.

In the stage of decline the symptoms gradually diminish in severity and the cough finally ceases.

For some time following whooping-cough the paroxysmal cough returns with each cold the child has or with sudden laughing or crying. Although this simulates the milder stages of whooping-cough, it is not contagious.

**Complications.**—The commonest complications are connected with the respiratory system. A large proportion of the deaths are due to bronchopneumonia, especially when associated with rickets. This is, of course, more frequent in the winter and spring months when the respiratory diseases are prevalent. During the pneumonia the paroxysmal cough often disappears. Emphysema may complicate the disease and is sometimes fatal. During the convulsive stage children are especially susceptible to the tubercle bacillus. Tubercular infection, which up to this time had been localized and held in check by the natural resistance of the child, may become active because of the child's weakened condition and exhaustion.

Hemorrhages may be regarded as the result of increased intravenous pressure, and the symptoms they cause depend, of course, upon the location of the hemorrhage. Epistaxis is the most frequent variety. Intracranial hemorrhages are infrequent, but a few cases have been reported which died as a result of the bleeding from the meningeal artery.

Endocarditis rarely complicates whooping-cough, but if pres-

ent makes the course of the disease more severe and the outlook more doubtful.

Convulsions are relatively frequent complications during infancy and should always be considered serious.

Diarrhea is also a frequent complication in whooping-cough during the summer, and is almost as serious as the respiratory infections during the winter. It depends, of course, in most cases upon the cleanliness of the milk-supply.

With the exception of the characteristic paroxysmal cough and whoop, the physical examination shows nothing abnormal in the uncomplicated cases except signs of enlarged peribronchial lymph-nodes. These are often evidenced by a D'Espine sign and are shown in the *x*-ray. The signs may be very pronounced and simulate peribronchial tuberculosis. They are temporary, however, and disappear with the disease.

**Blood.**—There is often a leukocytosis of 15,000 to 25,000 cells, which is greater than is found in any other afebrile disease. There is also an increase in the lymphocytes at the expense of the leukocytes, and are said at times to be as high as 80 per cent. The writer has never found a lymphocytosis or high white count in the early stage of the disease when it could be of value in making an early diagnosis.

**Pathology.**—There are no characteristic postmortem lesions of whooping-cough. Bronchopneumonia, however, is the commonest complication seen by the pathologist. Even without bronchopneumonia the peribronchial lymph-nodes are often enlarged, as in measles. The only lesion which may be said to be constant is that described by Mallory and his co-workers. They found that the ciliated epithelium of the respiratory tract is denuded in places and the cilia plastered down to such an extent as to interfere with a free removal of mucus. It is assumed, therefore, that the severe and prolonged paroxysms of coughing are necessary to forcibly dislodge and expel this mucus.

**Diagnosis.**—A positive diagnosis is made when a typical paroxysm is heard, or by isolating the infecting organism, the Bordet-Gengou bacillus, from the white glairy mucus. A paroxysm of coughing may often be induced by pressing the thumb

over the trachea. There are many cases that run such a mild course that even during an epidemic it is difficult to say positively that the patient has pertussis. One should, however, always suspect a child who coughs more frequently at night than during the day. The gradual increase in the symptoms and the failure of ordinary drugs to alleviate the symptoms should also arouse suspicion. The pertussis bacillus cannot be differentiated morphologically from the influenza bacillus. Unlike the influenza bacillus, however, it is possible to grow it on a media free from hemoglobin. There are no serologic means up to date of making a diagnosis in man. Agglutination and complement fixation are equally unsuccessful. Fortunately for the reputation of the medical profession, the diagnosis is usually made by the family before the physician is called in.

**Prognosis.**—The prognosis depends upon the age of the patient, his general physical health, the time of the year, and the physical surroundings and care. The younger the patient, the more serious the prognosis. One-quarter of the infants contracting the disease during the first year of life die. After six or seven years of age there is a relatively low death-rate. The prognosis varies with the severity and character of the symptoms and is always more serious when there are complications. It is important to bear in mind that whereas the immediate prognosis may be good, pertussis, next to measles, predisposes to tuberculosis more than any other disease.

**Prophylaxis.**—Since pertussis is a contagious disease, those suffering with or exposed to the disease should be isolated. Quarantine should be established for at least six weeks and in some cases longer. They should never be allowed to attend school or to travel in public conveyances. Parents often selfishly or unwittingly take them on journeys in trains, thus exposing many other children. No adequate means of stopping this practice has as yet been devised by our public health officers.

**Treatment.**—A plentiful supply of fresh air helps reduce the number of paroxysms. During the summer this method of treatment may be carried out even with the most delicate infants, but during the winter it should be practised with the

greatest care. A change of climate is often of great value, especially in the winter, if the child can be transported to a sunny, warm seashore without danger to others. It is said that an ocean voyage is often followed by remarkable improvement.

The diversity and number of local applications advertised and recommended is sufficient proof that they are of very little or no value. Inhalations, on the other hand, are often of real value. While there is any elevation of temperature at all the child should be kept in bed. A depressant or opiate should be given to prevent exhaustion, and must be given in large enough doses to obtain a physiologic effect. At times it may be necessary to push the drug sufficiently to cause prolonged sleep. This, of course, is attended with danger and should be considered the lesser of the two evils. Any opiate may be used provided it is effective and does not disturb the digestion. Sodium bromid or codein in doses suitable for the age are often quite satisfactory.

The diet should have considerable care and thought, and only those foods given which are best adapted to the child's digestion. In some instances dry foods, such as the starches, bread, cereals, etc., are indicated, and in others milk and eggs, etc. Since there is a considerable loss of food during a paroxysm of coughing, more food should be given to replace that which is lost. It is usually better to replace the food very soon after the vomiting so that it will be settled before the next paroxysm.

The continued coughing and retching often tires the abdominal muscles to such an extent that coughing causes pain. This may often be alleviated by applying a well-fitted abdominal belt.

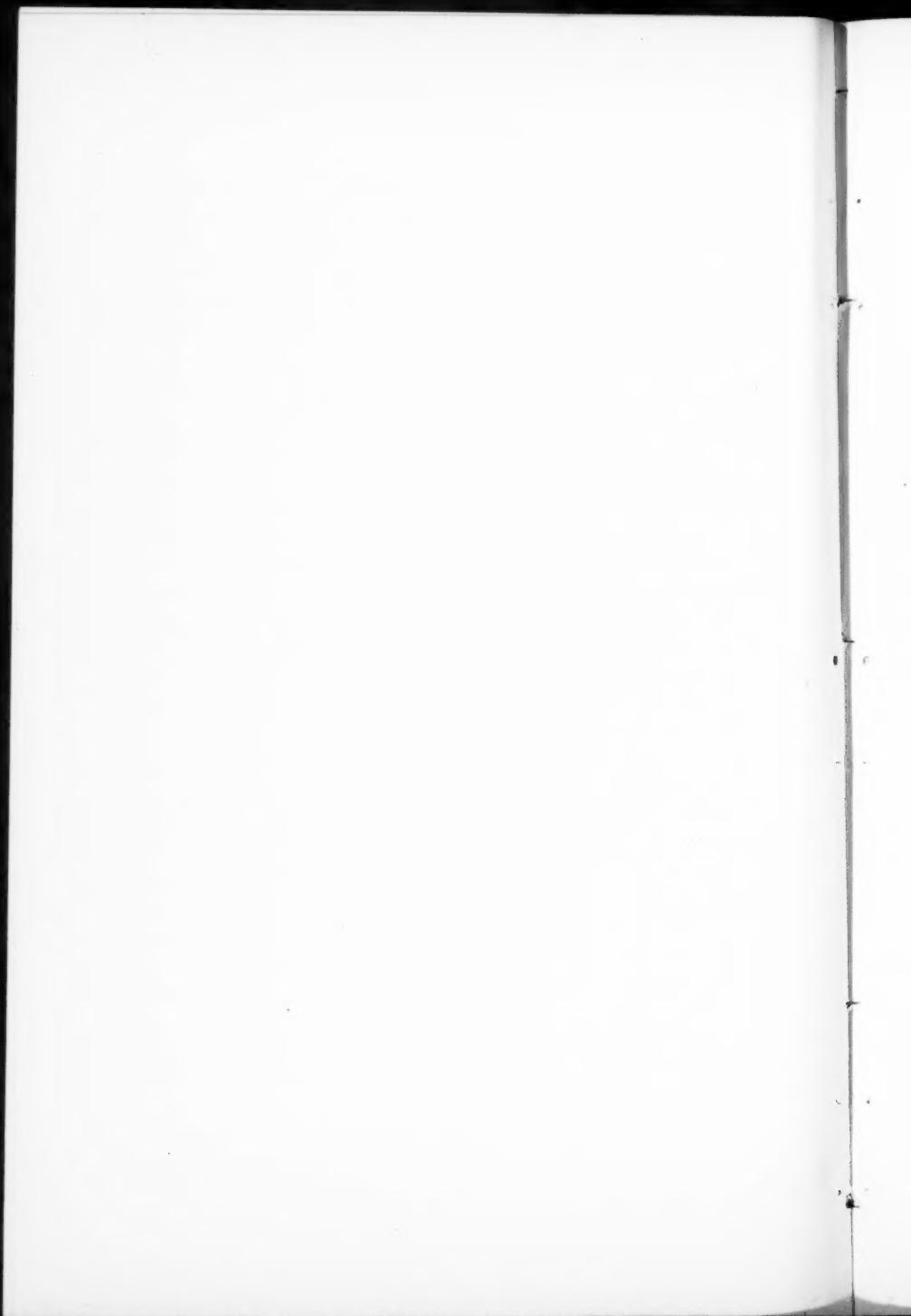
**Vaccine Therapy.**—There is a considerable difference of opinion at the present time as to the value of vaccine therapy in pertussis. It should be considered from two points of view—prophylactic vaccination and curative vaccination. The consensus of opinion seems to be that prophylactic vaccination against pertussis is of very definite value. The lack of satisfactory results in many cases may be due to the age of the vaccine. Huenenkens<sup>1</sup> has pointed out that vaccine should be

<sup>1</sup> Huenenkens: Amer. Jour. Dis. Children, 1918, xvi.

employed very fresh and without any preservative to be of any value. By fresh vaccine he means vaccine one week old. The loss of strength of the vaccine as it grows older is illustrated by the fact that vaccine two to three months old employed in very large doses, that is, 1,000,000,000, usually immunizes only about  $12\frac{1}{2}$  per cent. of the cases, while vaccine two to four weeks old confers immunity in 25 to 75 per cent. of the cases. Thoroughly fresh vaccine given in the same doses gives antibody formation in 94 per cent. of the cases, and when given in still larger doses—1,500,000,000 to 2,000,000,000—immunity is obtained in practically all cases.

Curative vaccination has been less satisfactory in the opinion of most clinicians, and the evidence for its use is less convincing than for early prophylactic vaccination. Apparently the best results are obtained when the vaccine is used very early in the catarrhal stage of the disease; less satisfactory results are to be expected in the later stages of the disease. The freshness of the vaccine, according to Huenenkens, also plays an important part in the results obtained in curative vaccination. When curative vaccination is employed during the catarrhal stage of the disease one expects that the paroxysms will be less frequent and the convulsive stage shortened. So far as the writer knows there never has been any serious results from the employment of pertussis vaccine either as a prophylactic or a curative agent. The dosage used depends upon the age of the child. In order to attain immunity children over two years of age should receive the vaccine every other day for three to four doses, commencing with 1,000,000,000 and increasing up to 2,000,000,000, unless the symptoms contraindicating its use appear. On the first injection 1,000,000,000 may be given; the second, 1,500,000,000; the third, 2,000,000,000, and the fourth, 2,000,000,000. In children under two years of age, especially delicate infants, half this dosage should be used. Inoculation of foreign protein in animals has taught us that when a foreign protein is given at intervals of ten days sensitization will result, but when given in shorter intervals, one or two days, immunity results. Since our object in using vaccines in pertussis is to attain

immunity the two-day interval is desirable. My own experience in the use of vaccine has been more favorable than unfavorable even with vaccine that is not as fresh as that which Huenenkens recommends. Cases have come under my observation in which a mixed vaccine has been used in the treatment of whooping-cough, but it has been shown to have no advantage over a straight pertussis vaccine.



## CLINIC OF DR. STANLEY COBB

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### THE TREATMENT OF THE PSYCHONEUROTIC

MUCH interest has lately been centered around those psychopathologic conditions variously known as "psychoneurosis," "nervous prostration," "psychasthenia," or "neurasthenia," and this awakening of interest has shown that these disorders are the commonest problems that the physician is called upon to meet. Whether modern life with its hurry and stress has actually increased the number of emotional breakdowns, or whether, through our better knowledge, we are recognizing more cases, is an undecided question. The truth probably lies between the two. Be that as it may, the fact is that our dispensaries are overrun with these sufferers and our wards are full of them, yet in spite of the commonness of the problem most physicians avoid the therapeutic issue, rule out obvious organic disease, and send the patient away unrelieved. This attitude of the profession is due fundamentally, I believe, to the fact that most doctors have no organized plan of attack on these cases. It is just such an organization of methodic treatment that I wish to outline in this clinic.

#### CASE I

A housewife of thirty-four was admitted to Dr. Edsall's service (East Medical, No. 231658) on July 14, 1919, complaining of indigestion. The routine history and physical examination may be abstracted as follows:

**Family History.**—Unimportant.

**Marital History.**—She has been married sixteen years, her husband is five years her senior; there have been 3 children, one of whom died of diphtheria at the age of ten; the other two are living and well. There was one miscarriage eleven years ago.

**Social History.**—Satisfactory living conditions, at present spending the summer on a large country place in the Berkshires where her husband works as gardener.

**Occupational History.**—Housewife for sixteen years.

**Past History.**—Diphtheria at eleven and measles and pertussis as a child. Her appetite has never been good, her bowels were regular up to the beginning of the present illness, and her average weight was 98 pounds up to one year ago, since when she has lost 14 pounds. Her only exercise has been her house-work. She sleeps poorly, as a rule, and has always considered herself of a "nervous make-up."

**Present Illness.**—The indigestion began four months ago, with sour eructations, heartburn, and belching one-half hour after meals. There was some epigastric distress, relieved by belching up gas, but no pain. These symptoms were at times relieved by charcoal and soda tablets. During the last three months she has been very apprehensive about her indigestion, she has felt weak, and has given up her work. At times she has been melancholy, thinking that she was not going to get better, and has had frequent dreams on the same theme. She has sweating and tingling of her hands and slight tachycardia when belching. The bowels have been irregular; much catharsis has been used.

**Physical Examination.**—Small woman, fairly well developed and poorly nourished. General physical examination shows nothing abnormal except carious teeth and pyorrhea; coated tongue; the edge of the liver is palpable; palms of hands moist; hyperactive reflexes and pseudoclonus of ankles; slightly prolapsed and retroverted uterus, with cervical tear.

Temperature, 98° to 99.6° F.; pulse, 70 to 100; respiration, 20 to 25.

**x-Ray:** Intestines—gas in gall-bladder region. No definite evidence of stone. Gastro-intestinal tract shows ptosis.

**Laboratory findings:**

Blood—90 per cent. hemoglobin. White count, 6600.  
Smear normal. Wassermann negative.

Stool—negative.

**Mental Status.**—The patient lies in bed and talks easily, occasionally weeping when her children or her home are mentioned. Her mood is that of depression, and she says she feels melancholy now and has for the past three months. At times she is not unhappy, but she used to be happy and sing all the time. Orientation and memory are good. Her special pre-occupations are of interest: She thinks of dying and then weeps because she fears she will die and lose her boys; she also thinks of her boys dying, and dreams of her husband's death. No hallucinations, delusions, or ideas of persecution are elicited.

Another interview brings out that fact that she had melancholy spells five years ago after the death of her daughter. The present symptoms began in April. Since September, 1918 her father-in-law has been living in her house. He worked at a distance, so she had to get up at 5 A. M. to start his breakfast, whereas her husband worked nearby and could have breakfast at 7.30. She professes fondness for her father-in-law and says that the household situation is happy, and that all would be smooth if she only had her health.

**Etiology.**—The conspicuous symptoms in this case are depression and gastric distress. Her mental situation is something as follows: A woman of thirty-four with a past history of moderate health and good habits, except for a period of melancholy after her daughter's death, has her marital situation upset by the appearance of her father-in-law. This increases her burden of work materially, fatigues her, causes loss of appetite, and takes away much of her marital happiness, which has been to her the chief satisfaction in life. She keeps on working in spite of her distress, doing the work not cheerfully, but with a feeling of duty and self-pity. She thinks about dying, thinks how sad it would be if she died, and finally fears she will die. The ptosis and gas are probably due to the depressed mood with its reaction of depression on the vegetative nervous system, coupled with loss of weight and lack of exercise. But no one of these factors would have brought about the breakdown—the total burden born by the individual is always a complex of many factors. After facing the situation in this unsatisfactory and,

mentally speaking, unhygienic way for six months, she works herself into such a state of tension that she is unable to see the facts clearly or thrash her troubles out with any one; so, feeling thwarted and misunderstood, she takes to her bed and so evades the situation.

**Treatment** consisted of a common-sense description of how the emotions may affect digestion, using Cannon's work as a basis. This being accepted, the family situation was thrashed out and the Social Service Department was called in to see the husband and help in keeping the home life satisfactory by not allowing the father-in-law to live with them, etc. A tonic to help the appetite was given, diet and forced feeding to increase weight was advised, and she was told to exercise more, both generally out-doors and with special exercises in-doors, in order to overcome the visceroptosis. But the blame for the trouble was clearly placed on her self-pitying maladaptation to the family situation, so that she should no longer use her stomach as the scapegoat and the medicine as a talisman.

#### CASE II

This case is more complicated and needs a more careful analysis. A biologist and chemist from a college in Ohio, who has been spending the summer on Cape Cod, was admitted to Dr. Edsall's service (East Medical, No. 232092) in July, 1919. He complains of neuritis, indigestion, and nervousness. The routine record, in abstract, is as follows:

**Family History.**—Mother high strung and father nervous.

**Marital History.**—Wife cannot have children because of hysterectomy before marriage.

**Occupational History.**—Teacher and laboratory worker, always has worked in-doors over books, etc.

**Social History.**—Good living conditions.

**Past History.**—Scarlet fever as a child. At nineteen had a nervous breakdown and had to be tube fed because he was said to be out of his head. Since youth he has always had very frequent nocturnal emissions, which he thinks have dragged him down. He has always been in the habit of eating too fast and

too much. The bowels have been constipated and there has been some bleeding from hemorrhoids. He has had occasional vomiting spells, perhaps once a year, associated with constipation. His usual weight is 170 pounds; during the last year he has been losing weight, especially in the last four months, and he now weighs 127 pounds.

**Present Illness.**—Four months ago began losing weight and appetite, he had more constipation than usual, and began to be troubled with flatus and colicky pains which were relieved by passing gas per rectum. He felt "fagged out," but kept on exercising because he thought it would be good for him. Three weeks ago he began having a dull but severe ache in the left arm, later the left hand felt as if it were "asleep." The pain was severe enough to interfere with the patient's sleep.

**Physical Examination.**—The patient is a small, well-developed, but poorly nourished individual. A general physical examination of the whole body shows nothing except a ptotic abdominal wall. A special neurologic examination shows tenderness along the course of the left musculospiral nerve from the brachial plexus to the elbow. There is paresthesia and numbness of the first and second fingers of the left hand, and in a small area on the dorsum of the hand corresponding to the distribution of the musculospiral nerve.

No fever; pulse, 75 to 100; respiration, 20 to 28.

*x*-Rays show slight hypertrophic changes in the dorsal spine.

There is an indefinite shadow in the gall-bladder region.

The stomach is very low and atonic, the ileum is low and the cecum normal. The cervical spine is normal.

**Laboratory findings:**

Urine—negative. Stool—normal, no lead.

Blood—has normal red and white counts; hemoglobin 85 per cent., Wassermann reaction is negative.

A diagnosis of visceroptosis, neuritis, and psychoneurosis was made, but in order to get a better idea of the relative values of the different factors and to give the patient an understanding of his troubles, several long interviews were undertaken from the psychiatric standpoint. Thus the following facts were brought out:

The patient's father was a minister; officially they were fond of each other, but they were always arguing and taking opposite sides of every question. The mother was a vigorous, high-strung woman, able to do a great deal of work, whereas the father was often sick and had many minor complaints. The patient is interested in his inheritance and explains most of his troubles by saying that they are inherited from either the father or the mother. He is dogmatic in his views, and is conservatively religious; his main pressure of activity is toward reforming people, taking up new causes in which he "can forget his own interests" and play the martyr; he says he "would do anything to fight injustice." He enjoys asserting himself as a preacher, and spontaneously says that it makes him "forget the feeling of self-abasement" that has been his "curse."

Along with this evangelical personality is a history of great sex tension and conflicts. He masturbated in his "teens" and worried about it a great deal. When he finally controlled this at seventeen he began having emissions five or six times a week or even twice a night; this increased his worries so that he became seclusive and would go off alone and talk aloud to himself. He then began to think that people could see that he looked queer; this made him extremely unhappy and at eighteen he broke down with "nervous prostration" and was sent to a hospital for three months. Here his principal symptoms were sadness, fear, restlessness, ideas of persecution, ideas of reference, negativism, with refusal to eat, so that he had to be tube fed, and finally suicidal ideas and intentions.

After recovering from this he took up his life-work and was quite successful. He would have been happy if the continued emissions had not bothered him so much. He had a love affair at twenty-three, but did not marry because he had not money enough. Later he went with prostitutes occasionally, but without satisfaction, and finally he had two illicit love affairs with married women. One of them lasted almost a year, and during that time he felt keenly his moral conflict, but was happier than ever before because the sex tension ceased to bother him. Finally at thirty-five he married a woman whose uterus had been re-

moved, so coitus was unrestricted. His twelve years of married life have been happy and he has been successful in his work. The nervousness, bowel troubles, and indigestion have been kept in check by hygiene, exercise, and simple medicines until the winter of 1917-18, when he undertook to do two men's work on account of the war; that summer he had little vacation, dropped his good hygienic habits in order to work for the liberty loans and do other war work, and finally during the winter and spring of 1919 he found himself in his old-time state, feeling that he must work every minute and reform the world.

**Etiology.**—We have, then, an individual with an inheritance of great energy from the maternal side, who develops an antagonism to his father, becomes ambitious, but breaks down under the strain of facing the problems of puberty. In spite of the decidedly ominous features of the psychosis into which he was plunged, he was able to recover, but the depression of the breakdown left its mark in the form of visceroptosis, which was perpetuated by the sedentary life. This organic defect (in my opinion secondary to the mood depression of the psychosis) caused constipation and intestinal stasis that may explain the neuritis. The present breakdown with its somatic symptoms is not bad, but can be seen to arise directly from the old unhygienic psychology of compensating for a feeling of inferiority, for it was this desire to rush into the war work and not be considered a slacker, that added the final burden which brought on the break.

**Treatment.**—As has been remarked before, treatment and diagnosis in these cases go hand in hand. The thorough examination in the beginning did much to encourage the patient. The long discussions showed him how the sickness was really a logical development, when he was looked upon as an organism reacting badly to its environment. Finally, to more definitely fix this point of view, a diagram was made indicating the main dynamic forces which had affected him. In this diagram (Fig. 220) the length of time that the forces have played on him are indicated by the length of the lines, the importance of each force is indicated by the breadth of the line, and all are shown converging on his personality at the age of eighteen and again

at the age of forty-seven, to cause a breakdown. Thus the patient grasped the whole situation, and was able to take the specific directions (outlined below) as rational forms of treat-

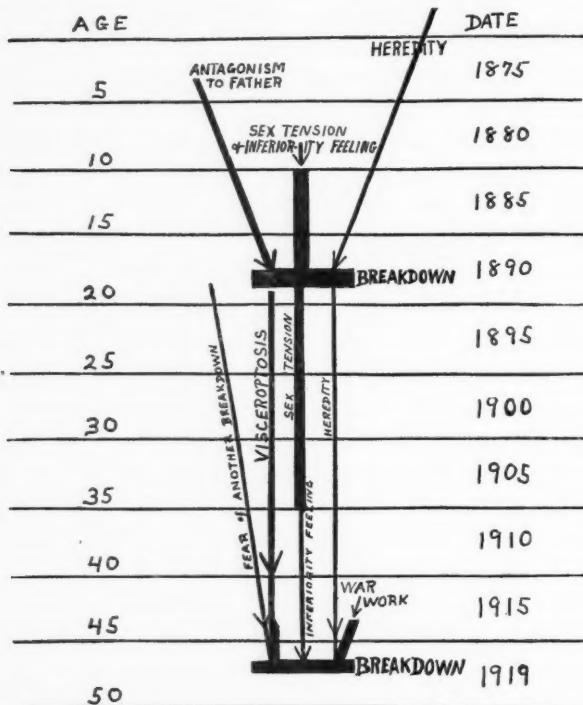


Fig. 220.—The diagram indicates in a dynamic way the psychopathologic factors which burden the individual, and by their concerted pressure cause breakdowns at certain times in life. The amount of importance attached to each factor is suggested by the breadth of the black line.

ment, not merely doctor's orders. For the time being, at least, he has been greatly relieved.

The directions given were as follows:

1. Wear orthopedic anteroposterior pad to help overcome ptosis and the resulting indigestion.

2. Put on weight by dieting and put on muscle by abdominal exercise to replace the artificial pad as soon as possible.
3. Take enough rest so that weight increases.
4. Take up golf and out-of-door pleasures.
5. Take mineral oil, cascara, and soda bicarbonate as directed.
6. Rest completely for two weeks and then get back to work in five weeks.
7. Remember that the inferiority feeling brought on the desire to overwork, causing the bad hygiene and the resulting symptoms. Try to look on the desire to play the reformer and martyr as a pathologic manifestation of the past poor facing of personal situations. Try to understand people and situations rather than judge them. Thus cultivate a more placid personality.

### CASE III

This case presents a somewhat different problem. A single woman of forty-one was admitted to Dr. Taylor's service in September, 1919. The records follow:

**Family History.**—Mother and father living and well, both are over seventy years old. One brother is nervous, two sisters are living and well.

**Social History.**—The patient has been a burden on her mother and father all her life (Fig. 221). The mother is an unusual, aggressive person and has trained the children strictly; she reads much and is discontented in the rural community. The father is easy-going and unable to hold a steady job. He has never handled the family situation. The house is isolated; it is small, disorderly, out of repair, five rooms, but clean. Their income is from the father's chores for neighbors and the mother's taking in washing.

**Past History.**—See Fig. 221. (The history as taken down routinely is merely a recital of various symptoms.)

**Present Illness.**—Gradual onset two years ago caused, in the patient's opinion, by her attempting to walk when she was too weak and did not have any support for her back. She did not actually walk, but threw herself from one support to another, and thus she "pulled out" all the nerves and muscles in her back.

## LIFE CHART.

AGE	SYMPTOMS, ETC.	INCAPACITY (in block.)	PERSONAL.	DATE
1			Born in Conn. on farm	1876
2				75
3	Whooping cough		Sister born.	1880
4			Mother frequently has "stomach and liver trouble."	81
5	Scarlet fever		Obeyed mother completely, never asserted herself.	82
6			Father always bothered with lame back.	83
7	Chicken pox		Sister born.	84
8			Began school.	85
9				86
10	Stomach trouble, began taking medicine.		Moved to New Hampshire	87
11	Fell from swing, in bed one day.			88
12	Menses			89
13	Stomach trouble increases			1890
14	Menstruation begins. Menorrhagia.		Left school because of ill health.	91
15	Medicines for "female weakness."		Occupied with sewing and fancy work.	92
16	Dysmenorrhoea with headache and vomiting.		Watched by mother and invalidised.	93
17	Headache and vomiting increase.			94
18	Retroversion treated with tampons, etc.		Light housework.	95
19	Leucorrhoea			96
20				97
21	"Curvature of spine discovered." Plaster jackets for 9 months.			98
22	Gripe.		Stopped all housework.	99
23	Insomnia and tremor of whole body.			1900
24	Broncho-pneumonia.			01
25			Younger sister married.	02
26				03
27	Exhaustion, smothering spells and palpitation, in bed 3 months.			04
28				05
29	New curvature and plaster jacket.			06
30			Older brother married.	07
31	In bed 6 months.		Younger sister married. Alone at home with mother and father.	08
32	Tubes, ovaries and appendix removed causing menopause.		Inspired to write songs. In county hospital.	09
33	Furunculosis. Headaches and vomiting			1910
34	Become continuous instead of with menses.		No work but composing songs.	11
35	"			12
36	"			13
37	Worse "Boils."			14
38	Drawing pains across abdomen and hips.			15
39	Exhaustion, can only stand 3 minutes. Stiff neck.			16
40	Stiff knees and back. Weight 120.		Plans to sell songs.	17
41	Fell down, in bed ever since. Leucorrhoea and backache ever since.		In county hospital. Nursed by mother.	18
42	Dysuria, urgency and loss of control. Gas on stomach.		In county hospital M.G.H.	19

She now has "drawing contractions" beginning in the neck and spreading down to involve the bowels, thereby causing her to throw from one side to another. The back is "so weak that it lets the bowels fall down." "Gas is thus generated, which rubs on the adhesions resulting from her operation and causes the pains." She complains of marked pains of greatly varying character in both legs, which, in combination with the neck pains, cause "yanking spells," *i. e.*, "drawing" the parts from side to side. There is much gas in the stomach constantly, and she can expel it at will. It bears no relation to meals, and leaves no taste in her mouth. The patient believes all her symptoms are due to weak back and to loss of nerve force consequent thereon. She desires, therefore, to have especially adapted braces placed on the back, and then, with storing up of nerve force, she will get well.

**Physical Examination.**—Well-developed, very poorly nourished woman of apparently fifty years of age, lying in bed. Her neck is held rigidly and she is grasping firmly on to both sides of the bed. Skin moist and clear; hair on upper lip long and coarse; pupils widely dilated; marked pyorrhea, coated tongue, and ragged tonsils; breasts atrophied; spine straight and held rigidly; neck held so rigidly that patient always looks straight ahead, and in looking to one side never turns her head, but merely rotates her eyes.

Temperature, pulse, and respiration are normal.

Urine: Normal except for trace of albumin on two occasions.

Blood: Hemoglobin 70 per cent., otherwise normal.

$x$ -Rays of lumbosacral spine and hip-joints are negative.

**Neurologic Examination.**—Negative except for marked general atrophy of all the muscles of the body, most pronounced in extremities. Varying amount of spasm in both anterior lower leg groups with partial bilateral, permanent Babinski. Spasm and some contraction of right and left hamstrings with note-

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Fig. 221.—The center column shows areas of solid black where the patient was completely bed-ridden. The lines indicate partial incapacity, and the greater the incapacity, the closer together are the lines. For further description, see text.

worthy atrophy of quadriceps extensors and adductors. Arms wasted throughout.

Finger-to-nose test gave variable results, the most consistent being some coarse tremor of the right hand. But if the patient's attention is directed to anything, there is always tremor. While talking she uses hands and arms in quite normal, purposeful, entirely co-ordinated gestures.

The patient is oriented, but obsessed with her multiple ills. When first seen she talked steadily for twenty to thirty minutes about these troubles, the order of their appearance, and the great number of physicians seen. Regardless of how approached, she soon brings up this topic. Practically her whole life has been spent in thinking about these numerous ailments.

**Progress Notes and Consultations.**—10/6/19: History of ovariectomy at thirty-two, with hot flushes for two years; in connection with the abnormal hair growth seen at present indicates that glandular dystrophy is a factor. Recommend basal metabolism.

10/7/19: No evidence obtained of organic nervous disorder. Believe atrophy general and secondary to two years in bed. Recommend against lumbar puncture at present. Recommend systematic massage and muscular re-education; also forced feeding.

10/9/19: Some improvement, most noticeable in patient's own efforts; *i. e.*, feeding herself, is more quiet, and does not burst out into long story of her woes, and is taking up some other interest. Is now on massage daily.

10/17/19: Seems to be slight improvement. Continues to feed herself. For past two days has been up in wheel chair in fairly erect position. Sits holding herself rigidly most of the time and tends to slump into semireclining position.

10/20/19: Improving on régime. Basal metabolism test failed on account of patient's inability to co-operate. Advise trying it again. No patellar or ankle-clonus elicited. Feet held in position of "chronic Babinski," typical of hysteria. Recommend ovarian extract medication.

11/1/19: Basal metabolism done fairly satisfactorily. Shows a normal figure.

**Etiology.**—From the medical standpoint it appears that the symptoms are largely unexplained, so the case was attacked from the psychogenic standpoint. In the first place the patient was interviewed carefully and questioned about the environment in which the symptoms arose, and the facts were set down chronologically in the form of a rough life chart.<sup>1</sup> This is a chart divided into years of the patient's life with a column for symptoms, diseases, etc., on one side, for personal and social history on the other, and a central column in which black areas are placed to indicate graphically the periods of disability. The chronologic sequence of events is then clearly seen and the relation of the personal and social aspects of the case to the symptoms is brought out.

With this chart in front of us we get an entirely new aspect of the case and can reconstruct the patient's life to explain the symptoms. A girl born on a farm, the oldest of three sisters. Her mother dominated the household, while the father was easy-going and incompetent. Early in life she showed signs of being physically weak and mentally passive, for she allowed the mother to dominate her in a way the other children did not tolerate. Her first symptoms began at ten, and she is vigorously doctored by her mother; at fourteen menstruation sets in, and she is frightened by the profuse flowing and more frightened by the medications given her for female weakness. At this early age she leaves school and is never again a normal member of the community. Her symptoms increase as her personal activities decrease. At eighteen she is given ill-advised local treatments for "retroversion," and these are followed by leukorrhea. At twenty-one another doctor finds curvature of the spine and puts her into plaster jackets for nine months; this turns all her attention on to the fall from a swing at eleven, which up to then had been forgotten. The symptoms kept on in spite of treatment and were especially bad at the times of her periods. Then, in

<sup>1</sup> Similar but more detailed life charts are used by Dr. Adolf Meyer in his psychiatric work. It is from him that the idea was taken.

1908, her youngest sister is married and she is left alone at home with her parents. The chart shows that she reacted to this situation by spending six months in bed. Again the doctors intervene, this time telling her that she "has been poisoned by her ovaries for years," so an operation is performed and tubes and ovaries removed. This is promptly followed by artificial menopause with all its discomforts. The symptoms, instead of disappearing, become constant, whereas formerly they were largely associated with menstruation. By this time she is spending most of her time in bed, has given up all work, and takes to writing poems. These are all on themes connected with love, marriage, children, and companionship—fantasies of those things in life which the patient has entirely missed. In 1917 she was urged to exert herself a little more than she thought right, she fell to the floor, was put to bed, and has stayed there ever since, with increasing symptoms of muscular stiffness, backache, dysuria, etc. From an organic standpoint the elderly appearance, atrophy of the breasts, and hair on the face can be accounted for by the artificial menopause ten years ago. The muscular atrophy is explained by disuse. The pain in the back, joints, and muscles may be partly due to toxic absorption from the tonsils and pyorrhea; and from the history of years of exaggeration of symptoms we are justified in assuming that slight pains from such a source may well be the basis of the marked rigidity and spasms seen in the neck, back, and legs.

**Treatment** of such a chronic case is, of course, difficult, and a cure is not to be expected, but we must remember that *any improvement* is worth working for, and the point of view must be taken that *all* of these patients can be helped. The method of procedure is different from that outlined in the other two cases. It is obvious that a person so long fixed in one rut of thought cannot accept a straightforward explanation until headway has been made by other means. Dr. E. L. Richards, of Baltimore, has recently published a paper (in the Archives of Neurology and Psychiatry, October, 1919) on the "Invalid Reaction," and I cannot do better than quote her outline of treatment: "The patient was then given a frank report of the results of the various

examinations, and was invited to think of his incapacitation, not as a disturbance in functioning of his gastro-intestinal tract, or some other point of visceral strategy from which his symptoms seemed falsely to emanate, but to think of it as a disturbance in the behavior and activities of his whole personality; he was urged to think of his symptoms as substitutes for reactions to unhappy experiences, thwarted ambitions, petty jealousies, romantic disappointments, an empty and dissatisfied life, a desire to escape marital or domestic responsibilities, or whatever the specific facts may be. While the patient was being encouraged to educate himself in this concept, he was given the benefit of any hygienic lifts suggested by the various examinations, such as attention to the weight curve, hemoglobin, eye-strain, etc."

"Equally essential as a reconstructive factor is the ward routine, arranged so that the patient gets a full and well-ordered but not an ostensibly planned day. Following breakfast in the dining-room there are two hours in the gymnasium and hydriatic department. The afternoon is broken into by the occupation class of an hour or more in weaving, basketry, carpentry, book-binding, etc., varied according to season and time by outdoor games, dancing and parties in the recreation hall, on the roof-garden, or time spent on the campus. Between scheduled hours there is opportunity for the patient to sew, crochet, embroider, write letters, read current magazines, daily papers and library books, or to lie down if she chooses. These concrete activities not only form a sort of natural bridge between the self-limitations of the invalidism and the return to normal action and interests toward which the patient is headed, but they also restore confidence in his somatic capabilities in general, and especially in certain viscera against which he has so long nursed suspicions of incompetence. He becomes stealthily aware that he can eat proteins, carbohydrates, and fats without disaster; that he can use his eyes without headaches; that he can exercise without fatigue and join a noisy frolic without collapse. And, with the knowledge that he can, comes usually the desire to do. The entire process of better adaptation is helped along by a

conscientious sensible survey of the facts of the case with the physician, usually in personal interviews in the physician's office, reviewing the daily events, reactions, and the observations by the nurses, giving consideration to the patient's complaint and problems, and removing them from the domain of *vague self-indulgence* to a reduction of concrete events and problems of the present, past, or future. So much for the method of practical approach which has been employed with these patients." Of course, Dr. Richards was working under ideal conditions in a psychiatric institute where all forms of therapy were easily available, but even without these appliances we can all do much.

To recapitulate: Treatment consists of taking the total personality of the individual into consideration and treating all aspects of the case.

In the first place the *painstaking physical examination* is important, for besides giving the physician much data to work with it gains the confidence of the patient and causes him to give weight to the physician's statements concerning psychogenic symptoms. Second, a *detailed history* is to be taken, preferably arranged in some tabular form so that the various events of the patient's life stand out in their true relationships. An example of this is the life chart presented in Case III. Routine histories, though well taken, are not sufficient for these cases. A really thorough conception of the development of the individual must be gained in order to understand the breakdown. And this material is not only useful from the standpoint of etiology, but very important to work over with the patient in order that he may grasp the broad point of view that his trouble cannot be blamed on one organ, but must be attacked from many angles.

The patient must be truly co-operative if he is to give the right sort of history; to gain this co-operation the physician must keep an objective attitude, for the patient must have the assurance, by word and action, that nothing in human behavior can either bore the physician by its triviality or surprise him because of its appearance of immorality. Anything that the patient may say must be listened to and accepted as evidence

that may throw light on the genesis of the symptoms. Nothing spoils the patient's co-operation more completely than a judging attitude which allows him to feel that the doctor considers that he is imagining pains or exaggerating. These aspects are only to be discussed after the doctor has evidence to show which can prove such contentions on his part. With this objective attitude to face, the patient usually brings up a great deal of useful material which is to be gone over and understood both by patient and physician. This method of approach may be called psycho-analysis, and, in fact, it is when thoroughly carried out. But I prefer to use the term *personality study*, thus using what is obviously good in the Freudian method, but avoiding its useless jargon and often harmful symbolisms.

If the patient is unable to talk freely and presents a wall of amnesia, the method of attack must be less direct. Under such circumstances a series of dreams often gives a clue to the underlying trends of thought which are important in the understanding of the situation. But I have seldom seen any useful purpose served by the intricate analysis of a single dream. The association test<sup>1</sup> is another method of approach to a difficult case and sometimes gives the examiner a most startling clue to the trouble. But more often little is learned from it except a general view of the patient's reactions, which have already been obtained in the history.

Third, with the complete history and physical examinations in hand, each symptom must be taken up and considered with due judgment to decide whether they need medical, surgical, physical, or psychologic therapy. If any of the first three are decided upon they are to be carried out according to usual practice.

The **psychologic treatment** is already well under way, for the history and physical examinations have usually cleared up many points and relieved the patient's mind of numerous fears. More complete success depends on the doctor's ability to give the patient a clear understanding of the etiology of the trouble.

<sup>1</sup> For a description of this test see S. I. Franz's new book on "Mental Examinations" or White's "Outline of Psychiatry."

This is often difficult and sometimes impossible; but if the physician will take an attitude of intelligent interest, listen attentively to whatever the patient produces and dispassionately view it as human behavior, this in itself will help a great deal. Most of the failures come because the physician projects into the situation his own emotional judgments and thus spoils the value of his observation, just as surely as he would spoil the value of a laboratory experiment if he allowed his personal desires to affect his observations. For example, the humorous attitude that many sufferers with "neurasthenia," "psychasthenia," and the like are "just plain fools" is purely a judging point of view, and worthless, if the object is to help the patient.

Even those of us who try the hardest to keep an objective attitude often reach the limit of endurance and protect ourselves from admitting our failure by calling the patient hard names. Most of us are in too much of a hurry, and the patient quickly senses it. The all-too-common jocose reassurance that "There's nothing the matter with you" is so obviously false from the patient's point of view that she makes up her mind that physicians are stupid and goes to the faith healer or sympathetic chiropractic.

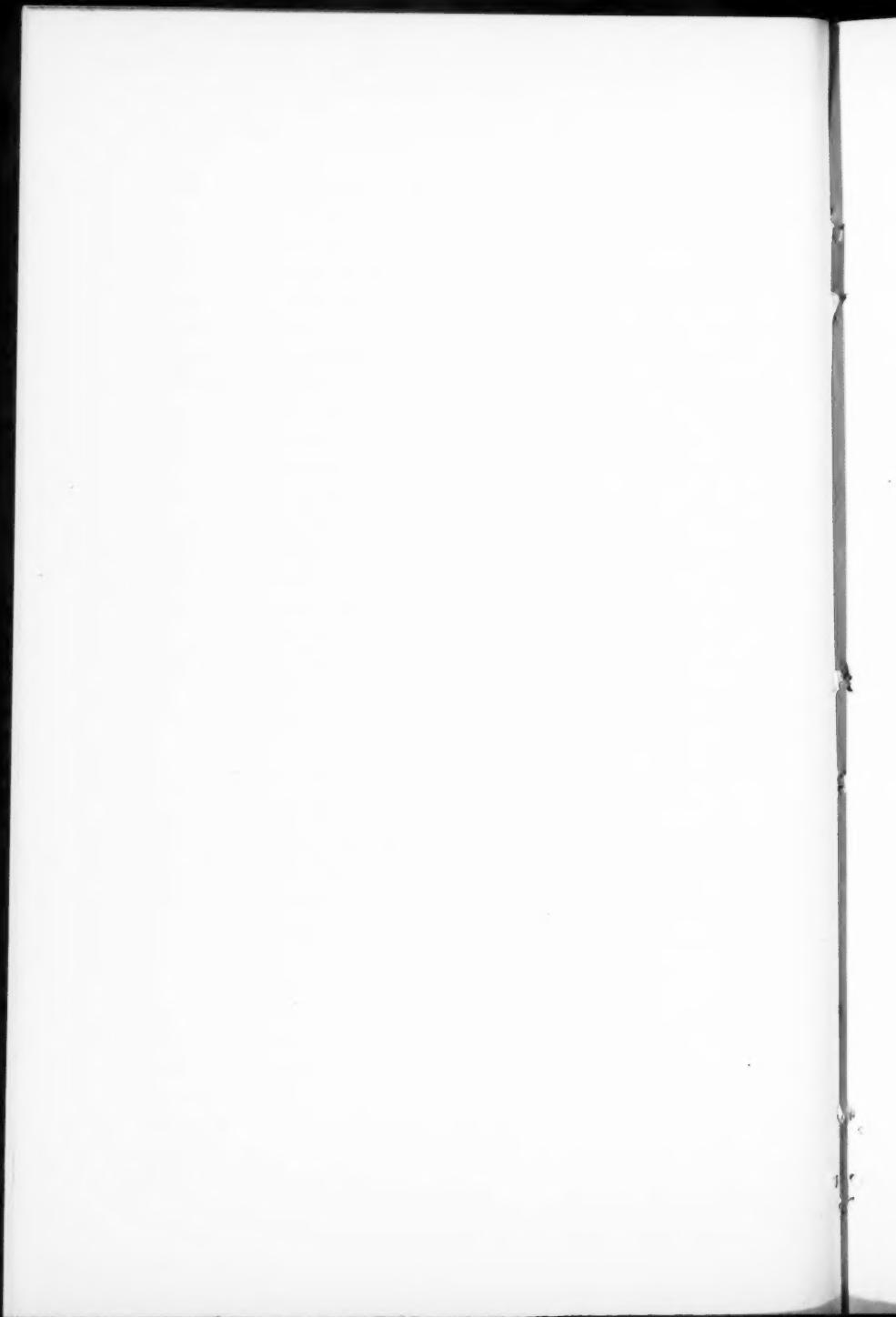
Besides the general personality study and frank explanation to the patient, each individual symptom must be explained as well as possible on a physiologic basis. The fundamental instincts and their resulting emotions can be explained, and such common symptoms as palpitation, flushing, diarrhea, and gastric distress can be clearly shown to arise from the emotions. In other words, the patient is taught enough rudimentary psychology and physiology so that she can understand the facts brought up in the history.

The prognosis in such cases as those cited varies directly with the social situation and the adaptability of the patient. Such being the case, it is impossible to cure many of them, for their environments cannot be changed and their past histories cannot be erased. But there is just one worth-while point of view: *all* can be *helped*, so let us do the best we can.

The matter of diagnosis has been purposely slighted in this clinic because too often the psychiatrist considers this all im-

portant, neglecting really to record the facts of the case and treat the patient.

The trend of modern psychiatry is to use long names and complicated classifications. It is hoped that the cases cited above will in a measure show that a common-sense and intimate study of the individual personality is what is needed, and that after this is carried out the case will naturally fall into one of the large and easily understood classes of typical human behavior.



## CLINIC OF DR. LESLEY H. SPOONER

MASSACHUSETTS GENERAL HOSPITAL

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### LABORATORY DIAGNOSIS

**Practical Benefits to Be Derived from the Use of the Laboratory as a Help in Diagnosis; Importance of Members of the Profession Familiarizing Themselves with as Many of the Methods of Laboratory Investigation as Possible. Significance of the Various Tests and Reactions and Descriptions of the Same.**

A SCORE of years ago the laboratory of the average physician consisted of a shelf in any remote and dark closet on which reposed a few dust-covered reagent bottles and a rack of partially filled and damaged test-tubes. Since that time a great evolution has taken place, not so much in the laboratories of our large hospitals and universities, but more especially in the minds of the medical profession.

The importance of the laboratory as a help in diagnosis is becoming now so well recognized that it is perhaps trite to devote a chapter of this clinic to the subject.

I shall attempt to outline some of the practical benefits derived from such work, rather than to give any description of methods, which can be obtained from consultation of medical literature.

In these days of specialization, when it is becoming increasingly difficult for one individual to cover the field of medicine, it is necessary for the general practitioner to consult his specializing brethren upon many subjects. For this reason it is obviously the duty of the profession in general to familiarize itself with as many of the methods of laboratory investigation as possible.

Some of these can be performed easily by all, some require the special training of one devoting his entire attention to such study. The benefits should, however, be at the disposal of everyone.

Those who had the privilege of serving in the army during the recent war can appreciate the elevated standard of medical practice which results from a co-operation of the clinical and laboratory phases of medical science.

The routine examination of urine has long been employed in all large institutions because of the frequent discovery of albumin and sugar in the urine of patients not presenting suspicious symptoms. Such a procedure should certainly be recommended in general, except possibly in obviously trivial ailments. The examination of the sediment is, however, almost universally neglected. In one of my clinics this is performed as a routine regardless of the presence of albumin, which is most frequently taken as an indication for further investigation of the urine. Not infrequently the discovery of pus and blood in quantity insufficient to produce albumin serves as a great help in diagnosis.

The renal function test by means of phenolsulphonephthalein is now recognized as an easy and very satisfactory aid in prognosis of chronic nephritis. Although many diseased kidneys show a normal excretion, a diminution in the output of this dye seems to run parallel with the actual function of the kidney. Of late the test of Mosenthal, with its various modifications, has come into prominence. This, when scientifically executed, consists of determinations of the urinary solids in two-hour specimens of urine, excreted upon a fixed diet. Although the most satisfactory results are obtained from estimation of the sodium chlorid and nitrogen content, yet an approximate idea of renal function may be suggested by the fixation or non-fixation of quantity and specific gravity upon the two-hourly day and night specimens. In the diseased kidney this fixation is represented by a consistently low level of solid excretion, or at least a delay in response to the heavy meal of the day.

The examination of the blood is obviously of great importance in any obscure disease. The accurate estimation of the cells and

of hemoglobin is frequently not feasible in the busy life of the practitioner. The stained film is, however, in many instances a convenient substitute for the more laborious procedures. By means of this one is able to judge in a rough manner the presence of a leukocytosis which is of great aid in differential diagnosis between those infectious diseases in which is found an increase of white cells and those in which a leukopenia exists. It is to be borne in mind, however, that the actual count is necessary for absolute determination. The differential count frequently reveals the presence of an eosinophilia, so often associated with parasitic intestinal invasion.

In spite of the infrequency of the leukemias, such a count is of service in the determination of the etiology of adenitis.

In regard to anemia it may truthfully be stated that a more accurate measure of diminished hemoglobin can be reached by a study of the stained film than by the common, rough method of Tallqvist, although it is not safe in pronounced cases to depend entirely on either method. A further study of the smear serves as a valuable aid in the differential diagnosis of the two chief types of this disease. For these reasons it seems rational to recommend this as a routine procedure in all doubtful cases, steps to be supplemented by further laboratory study as the individual case indicates.

The diagnosis of malaria is too frequently made by the clinical symptoms alone. This is more particularly true in the South, where it is certain that this disease is far less prevalent than is indicated by rough statistics. It is obvious that the proper practice of medicine demands an absolute diagnosis, when such is so readily at hand, rather than the time-consuming therapeutic test. The blood film, stained by Wright's method, is the most reliable for the demonstration of the parasite.

At present Health Boards throughout the country are performing the test for tubercle bacilli in the sputum. The advantage of this from the standpoint of diagnosis and prophylaxis need not be considered. It is doubtful whether it is wise to recommend that this examination be undertaken by the practitioner, if such will cause the neglect of other laboratory in-

vestigations which are best performed by the physician, but it might be stated that this simple procedure, carried out by oneself, leads to a more accurate knowledge of the number of bacilli, which is often an aid in following open cases of pulmonary tuberculosis. Other analyses upon sputum will be considered under Bacteriology.

The examination of feces is notoriously neglected. It is unfortunate to note a tendency to accept the patient's diagnosis of "worms." The rule of the large hospitals to accept only ocular proof of parasitic invasion should be more widely diffused. Communication within this country and with our colonies has rendered importation and transplantation of certain parasitic diseases into communities in which they were formerly unknown. At present amebic dysentery and uncinariasis are to be found in all latitudes.

The examination of feces for ova by the method advised by Barbar is most simple and efficacious. This consists of a mixture of the material with a hypertonic saline solution which causes such concentration that the ova are found with ease. This method is applicable to hookworm, ascaris, and the tape-worms in general.

The Schmidt-Strasburger test diet is to be recommended as a relatively easy means of demonstrating functional and organic intestinal disease.

It is frequently impossible to confirm the early suspicion of malignant disease of the intestine by means of the *x*-ray. This is often suggested only by positive tests of occult blood.

Gastric analysis is an unpopular procedure in practice. Its discomforts can be eliminated largely, however, by the use of the Rehfus tube. Aspiration demonstrates not only stasis, but the presence or absence of free HCl, an important factor in diagnosis. The microscopic examination is serviceable in the determination of organic disease. The test-meal has fallen into some disrepute, so that it will be omitted from discussion, because it is my aim to emphasize only the accepted and vitally important tests.

The examination of body fluids is frequently of great importance in differential diagnosis. It is often by no means obvious

upon what disease process the formation of pleural or ascitic fluid takes place. The determination of the specific gravity and albumin is frequently sufficient to differentiate between the transudate and exudate. The latter can be performed with sufficient accuracy by the nitric acid test. More elaborate procedures are helpful, but generally not essential except in most confusing cases. The detection of the tubercle bacillus either by direct examination or animal inoculation is frequently possible in effusions.

The examination of spinal fluids in cases of meningitis is essential. Although no specific serum treatment exists for tuberculous and pneumococcus meningitis, that produced by the meningococcus—the so-called epidemic cerebrospinal meningitis—has been rendered a much less fatal disease by the administration of the specific serum. The microscopic study of the purulent exudate derived from the spinal canal shows the infecting organisms, which may, in the case of the pneumococcus and meningococcus, be cultivated at once.

The diagnosis of early syphilitic disease of the nervous system is often made through an investigation of the spinal fluid. In the active stages of tabes dorsalis, general paresis, and other syphilitic diseases of the cord and brain the spinal fluid, although clear, shows a lymphocytosis, an increase of globulin, and a positive Wassermann reaction. A determination of the extent of spinal irritation, as shown by these factors, is of service not only in diagnosis but also as a means of regulating treatment.

The colloidal gold reaction performed on the fluid is also of service in the differential diagnosis of the above-mentioned disease processes. A blood-free fluid is necessary in order to perform these tests, although a reliable reading of the Wassermann reaction may be obtained in blood-tinged fluid.

Not all these elements—cells, globulin, Wassermann, and colloidal gold—are positive in every case; but diagnosis can be made or confirmed in a high percentage of cases by one or more positive findings. As a general rule it might be stated that in paresis, blood and spinal fluid are positive; while in other conditions either or both may be negative. The frequency of positive

findings in spinal fluid associated with negative blood reaction indicates the necessity of this investigation.

The Wassermann reaction during the last few years has come into a prominence which it justly deserves. The public are becoming so educated that they are demanding it almost as a routine. The latter should be encouraged, since in this way it is possible to discover many cases of latent syphilis and to pronounce as syphilitic so many obscure symptom complexes.

In my experience in the army approximately 10 per cent. of apparently healthy individuals showed positive Wassermann reactions, confirmed in the majority of cases by subsequent blood tests. This investigation should not be limited to cases suspected of syphilis, but if possible be made a routine, and if not, utilized in all cases of doubtful medical diagnoses, regardless of the social status of the individual. The routine method was employed on all medical admissions in at least one of our base hospitals during the recent war as it is in most of our large civil hospitals. The application of this rule has revealed positive reactions in 5 per cent. of the routine cases not suspected of the disease in one of my out-patient clinics.

It is fortunate to note that the day of performing magical tricks upon one's patients is passing. The man of average intelligence is not only familiar with the significance of the test, but is well aware for what purpose the blood is being withdrawn. For this reason its employment as a routine has the obvious advantage of not arousing in the patient the idea of his suspicions in the mind of the consultant. This is not a reaction to be attempted by the general practitioner, not only because of the elaborate nature of the technic, but of the skill of the worker necessary for its interpretation.

Of the special tests, the tuberculin reaction is of great value in the early diagnosis of tuberculosis. Of the various methods, the subcutaneous administration of old tuberculin seems the most reliable. This requires constant regular observation of temperature and pulse.

The Schick reaction, as modified by Zingher, is most useful in determining susceptibility to diphtheria toxin. This is es-

pecially helpful in times of epidemic, since active immunity to the disease can be secured very easily by injections of toxin-antitoxin.

Bacteriology is a science of the last quarter of the last century. In its early life discoveries seemed to multiply by geometric progression, but progress has not halted even at the present time.

The necessity of the actual bacteriologic diagnosis of diphtheria is well known to all. Although strictly speaking this work should be limited to central laboratories, the requisites for such diagnosis lie more in the skill and experience of the observer than upon any elaborate apparatus.

Recent studies upon anaphylaxis make the medical profession averse to the indiscriminate use of serum, especially upon individuals possessing a natural hypersusceptibility, evidenced by asthma and various of the vasmotor diseases, and that acquired by previous administration of serum. Consequently, the use of serum is contraindicated in any doubtful case.

For the same reason it is unwise to administer serum as a routine in the treatment of pneumonia. Cole has shown that in only one group of pneumococci, *i. e.*, Type I, is the specific treatment efficacious. In that variety mortality is distinctly reduced by its administration. In my experience, covering over 1100 cases, this group comprises only about 25 per cent. Obviously, the bacteriologic determination of the variety of the infecting organisms becomes imperative. For this purpose it is necessary to deliver immediately to one competent to perform the test a sample of sputum from the lower air-passages, collected in any sterile receptacle. The procedure is more time-consuming than difficult, consisting of the injection of the material into the peritoneal cavity of a white mouse, the recovery of the organism from that site after twelve hours, and its agglutination with known sera of the first three types.

The blood-culture is by far too much neglected by the general practitioner. As a means of early diagnosis of typhoid fever it is of far greater value than the well-known Widal reaction. It is possible to recover the pneumococcus when associated with pneumonia and other infectious processes and the streptococcus

which has received so much mention in our recent journals. The demonstration of these organisms in the blood-stream has not only diagnostic but also a great prognostic value. In drawing the blood for culture the greatest aseptic precautions should be practised, for the presence of contaminating organisms must be avoided. The blood should be expelled from the syringe into the media at the bedside and the mixture sent at once to the laboratory.

The following suggestion is made as a matter of convenience: 100 c.c. of dextrose bouillon is run into a flat-sided 6-oz. bottle, cotton plugged, and sterilized. The plug is then saturated with boiling paraffin. Plugs thus prepared are easily loosened by heating the neck of the bottle in the flame of an alcohol burner, which serves also to flame the mouth of the bottle as an added precaution against contamination. The examination of the culture is the work of the trained laboratory worker and needs no further discussion in this article.

During the recent war considerable attention was drawn to Vincent's angina, a disease which occurred in considerable numbers in many of our camps. In association with this ulcerative condition of the throat, which has been confounded with syphilis, are found two organisms, the spirillum, which bears the name of the disease, and a fusiform bacillus. These organisms are readily detected in smears stained by any of the anilin dyes.

The demonstration of the *Spirochaeta pallida* is perhaps one of the most important of any of the laboratory procedures. Before the discovery of the etiologic factor of syphilis it was often customary to await the appearance of the secondary roseola before instituting the extensive treatment of the disease. Now it can be stated safely that the chances of cure are indefinitely multiplied if treatment can be initiated immediately after the discovery of the primary lesion. This can be done conscientiously only after the demonstration of the organism in the serous discharge from the lesion.

Since its staining properties are so poor, it is best recognized by means of the dark-field illumination. In skilled hands this is possible in all cases which have received no local medication.

The organism appears under high, dry magnification as a slender, actively motile, colorless spirillum.

In this article I have attempted to show, rather than detailed methods, the uses of the laboratory in diagnosis and practice of medicine. It is well understood that facilities and time are not at the disposal of all for the performance of many of these investigations. It is true, however, that the public is entitled to all such advances in medical science.